GE Healthcare

ÄKTAcrossflow

Instrument Handbook

ÄKTA™

Important user information

All users must read this entire manual to fully understand the safe use of ÄKTAcrossflow.

ÄKTAcrossflow is intended for laboratory use only, not for clinical or in vitro use, or for diagnostic purposes.

WARNING!

The WARNING! sign highlights instructions that must be followed to avoid personal injury. It is important not to proceed until all stated conditions are met and clearly understood.

CAUTION!

The Caution! sign highlights instructions that must be followed to avoid damage to the product or other equipment. It is important not to proceed until all stated conditions are met and clearly understood.

Notes

Note: *A Note is used to indicate information that is important for trouble-free and optimal use of the product*.

Recycling

This symbol indicates that the waste of electrical and electronic equipment must not be disposed as unsorted municipal waste and must be collected separately. Please contact an authorized representative of the manufacturer for information concerning the decommissioning of equipment.

WARNING!

This is a Class A product. In a domestic environment, it might cause radio interference, in which case the user might be required to take appropriate measures.

WARNING!

All repairs should be done by personnel authorized by GE Healthcare. Do not open any covers or replace any parts unless specifically stated in the instructions.

WARNING!

The computer should be installed and used according to the instructions provided by the manufacturer of the computer.

WARNING!

The mains power switch or other disconnect device must always be easy to access.

CE-certification

This product complies with the European directives listed below, by fulfilling corresponding standards.

A copy of the Declaration of Conformity is available on request.

- 73/23/EEC, Low Voltage Directive
- 89/336/EEC, EMC Directive

The CE logo and corresponding declaration of conformity, is valid for the instrument when it is:

- used as a stand-alone unit, or
- connected to other CE-marked GE Healthcare instruments, or
- connected to other products recommended or described in this manual, and
- used in the same state as it was delivered from GE Healthcare except for alterations described in this manual.

:Note: *The Declaration of conformity is valid only for systems that are marked with the* ***CE*** *logo:*

CE

Contents

1 Introduction

1.1 The Instrument Handbook 2
1.2 Installation 2
1.3 ÄKTAcrossflow system 3
1.3.1 System control 3
1.3.2 Instrument unit components 4
1.3.3 Rating label 5
1.4 Operating principles 6
1.4.1 Liquid flow path 6
1.4.2 Ultrafiltration (UF) 7
1.4.3 Microfiltration (MF) 7
1.4.4 Process optimization in 'total recycle mode' 7
1.5 Liquid delivery 8
1.5.1 Pumps 8
1.5.2 Valves 9
1.5.3 Reservoirs 11
1.5.4 CFF cassettes/cartridges 12
1.5.5 Detectors and monitors 13
1.5.6 Tubing and connectors 14
1.5.7 Fraction collection (optional) 17
1.6 Sanitization of the flow path 18
1.7 Associated documentation 19

2 Basic operation

2.1 Starting the system 21
2.2 Set-up the instrument 24
2.2.1 Selecting reservoir 24
2.2.2 Configuration of tubing kits for high and low flow applications 25
2.2.3 Kvick Start cassettes, cassette manifold and Kvick Lab Packet . 27
2.2.4 Hollow fiber membrane cartridges 33
2.2.5 Creating a method 37
2.2.6 Preparing the system 37
2.2.7 Running a method 37
2.2.8 After the run 38
2.3 Calibration 39
2.3.1 Calibrating the pressure sensors 40
2.3.2 Calibrating the pH electrode 40
2.3.3 Calibrating the conductivity cell 42
2.3.4 Calibrating the reservoir level sensor 45
2.3.5 Setting the retentate holdup volume 48
2.4 Stop the pumps 50
2.5 Shut down the system 50
2.5.1 Restart procedure 50

3 Maintenance

3.1 User maintenance schedule 52
3.2 User maintenance instructions 55
3.2.1 Cleaning the system 55
3.2.2 Feed pump, transfer pump and permeate pump 56
3.2.3 Membrane valves 58
3.2.4 UV flow cell 58
3.2.5 pH electrode 59
3.2.6 Conductivity cell 60
3.2.7 Pressure sensors 60
3.2.8 Sample inlet air sensor 61
3.3 Replacing spare parts 62
3.3.1 General instructions 62
3.3.2 Feed pump P-984 and transfer/permeate pump P-982 62
3.3.3 Membrane valve block 68
3.3.4 Rocker valve block 69
3.3.5 2-way transfer purge valve and pressure modulating/control valves R-PCV and P-PCV72
3.3.6 Pressure sensor PP and PR 74
3.3.7 Pressure sensor PT (pump outlet manifold) 75
3.3.8 Pressure sensor PF 76
3.3.9 Air sensor 77
3.3.10 UV flow cell 78
3.3.11 pH electrode 83
3.3.12 Conductivity cell 84
3.4 Priming the system 85
3.4.1 Manual priming 85
3.5 Preventive maintenance 86

4 Troubleshooting

4.1 Feed pump, transfer pump and permeate pump 88
4.2 Membrane valves 89
4.3 Pressure sensors 89
4.4 Pressure curve 90
4.5 Conductivity curve 90
4.6 UV curve 91
4.7 Air sensor 92
4.8 Installation Test. 92
4.9 Checking the pump pressure 94

5 Reference information

5.1 System description 97
5.1.1 ÄKTAcrossflow system 97
5.1.2 Indicator and switch on the instrument unit 98
5.1.3 Component location 99
5.1.4 Electrical connections 103
5.1.5 Mains fuse 104
5.1.6 UniNet-1 communication 105

5.1.7 System flow path106
5.1.8 Piston rinsing system109
5.2 Component descriptions 111
5.2.1 Pump P-982 and P-984111
5.2.2 Valves114
5.2.3 Reservoirs119
5.2.4 CFF cassette/cartridge122
5.2.5 pH electrode and cell holder123
5.2.6 Monitor UPC-980 and UV cell124
5.2.7 Conductivity cell125
5.2.8 Pressure sensors126
5.2.9 Air sensor 925127
5.3 Specifications 128
5.3.1 Technical specifications128
5.3.2 ÄKTAcrossflow component materials134
5.4 Chemical resistance guide and chemical compatibility 135
5.5 Ordering information 137

List of figures

Fig 1-1. The ÄKTAcrossflow instrument unit. 3
Fig 1-2. Location of components. 4
Fig 1-3. Layout of rating label. 5
Fig 1-4. The liquid flow path of ÄKTAcrossflow. 6
Fig 1-5. Tube connections on delivery. 15
Fig 1-6. Tube connections when the equipment is operational 16
Fig 1-7. Unit with bottles and resovoir. 16
Fig 2-8. Holder for flat sheet membrane cassette. 28
Fig 2-9. Flat sheet membrane cassette - Kvick Start. 29
Fig 2-10. Cassette manifolds. 30
Fig 2-11. Kvick Lab Packet Holder. 32
Fig 2-12. Holder for hollow fiber membrane cartridge. 34
Fig 3-13. Pump head, exploded view. 64
Fig 3-14. Pump head, exploded view. 66
Fig 3-15. Membrane valve block, exploded view. 68
Fig 3-16. Rocker valve block, exploded view. 70
Fig 5-17. The ÄKTAcrossflow instrument unit. 97
Fig 5-18. Location of ÄKTAcrossflow components. 99
Fig 5-19. Buffer bag holder. 100
Fig 5-20. Location of bottles. 101
Fig 5-21. Mains cables. 103
Fig 5-22. Liquid flow path 106
Fig 5-23. Piston rinsing system 109
Fig 5-24. Pump head, exploded view 112
Fig 5-25. Feed pump P-984 pump principle 113
Fig 5-26. Reservoir 350 ml. 119
Fig 5-27. Reservoir lid 120
Fig 5-28. The Kvick Start cassette. 122
Fig 5-29. The Kvick Lab Packet cassette 123
Fig 5-30. The hollow fiber membrane cartridge. 123

1 Introduction

This Instrument Handbook is intended for use with the ÄKTAcrossflow™ system.

WARNING! This instrument is intended for laboratory use only, not for clinical or *in vitro* diagnostic purposes.

The purpose of the ÄKTAcrossflow system is to facilitate process development and optimization of ultrafiltration/diafiltration (UF/DF) and microfiltration (MF) unit operations.

ÄKTAcrossflow is a fully automated system for Cross Flow Filtration (CFF), and uses flat sheet or hollow fiber membranes to separate components in a liquid solution or suspension based on their difference in size.

In CFF, the fluid is pumped parallel to the surface of the membrane. An applied Trans Membrane Pressure (TMP) serves to force a portion of the fluid through the membrane to the permeate side. Particulates and macromolecules that are too large to pass through the membrane pores are retained on the upstream side. However, the retained components do not build up at the surface of the membrane. Instead, they are swept along by the parallel flow.

ÄKTAcrossflow is designed and optimized for operation with the following membranes:

- Flat sheet membrane (50 cm^2 and 100 cm^2) in UF/DF applications.
- Hollow fiber membrane (40 cm^2 and 50 cm^2) in UF/DF and MF applications.

ÄKTAcrossflow features:

- Ultrafiltration and Diafiltration of proteins:

  Typical cut-offs: 3 kD to 500 kD.

- Microfiltration of cell and protein solutions:

  Typical cut-offs: 0.10 µm to 0.65 µm.

1.1 The Instrument Handbook

This handbook provides technical information and basic operating instructions for the ÄKTAcrossflow system. In addition, maintenance schedules, instructions for troubleshooting and user maintenance are included.

1.2 Installation

Important! The installation of ÄKTAcrossflow must be performed by personnel authorized by GE Healthcare.

1.3 ÄKTAcrossflow system

The ÄKTAcrossflow system comprises the following:

- ÄKTAcrossflow instrument unit
- PC (optional)
- Flat screen monitor (optional)

Fig 1-1. The ÄKTAcrossflow instrument unit.

1.3.1 System control

UNICORN™ software controls and supervises the ÄKTAcrossflow system. It runs on a PC with Microsoft™ Windows XP™ operating system, and includes hardware for interfacing the controlling PC to the liquid handling parts of ÄKTAcrossflow.

UNICORN controls the run data acquisition from sensors and monitors. UNICORN also evaluates results and generates reports.

1.3.2 Instrument unit components

The location of the components in the instrument unit is shown in the figure below.

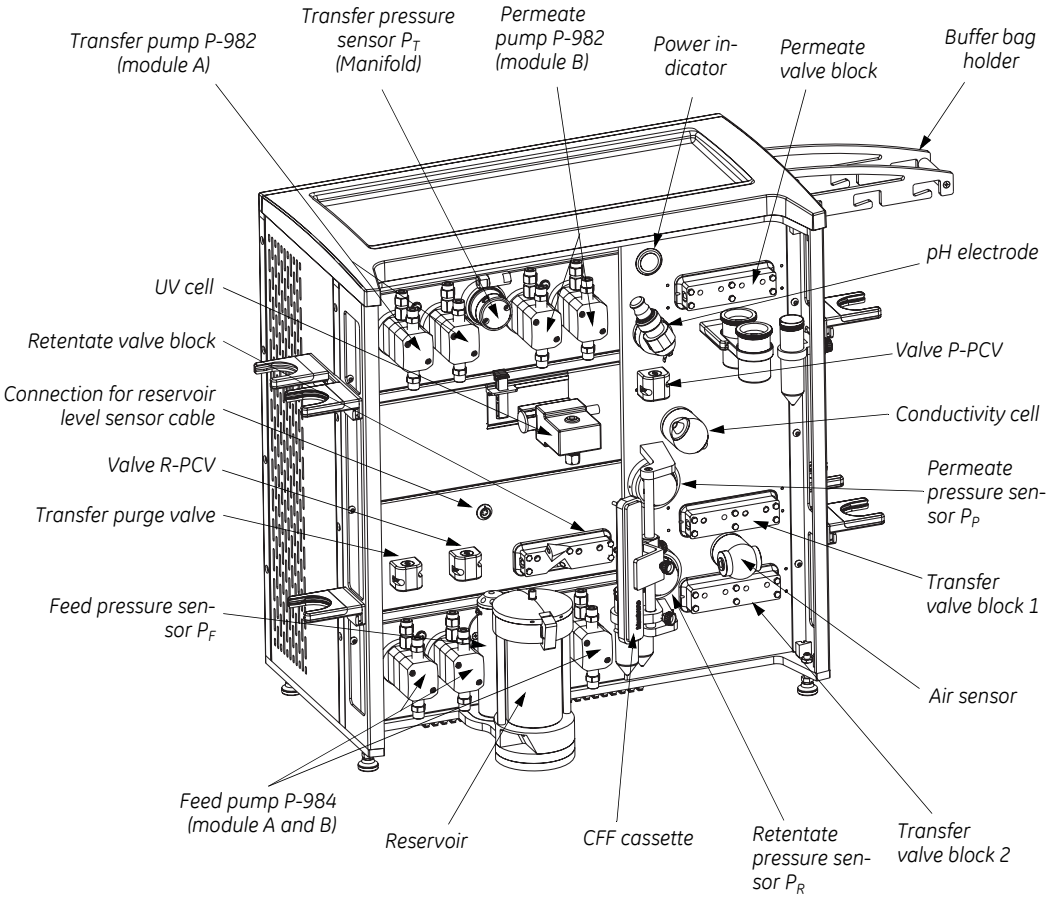


Fig 1-2. Location of components.

The main components are described in detail in the *Reference information* chapter of this manual.

1.3.3 Rating label

The rating label is located on the lower part of the instrument's rear panel (see Fig 1-3). These ratings determine the electrical hazards of the equipment connected to the supply voltage. There are, however, other hazards that might be more severe, see *ÄKTAcrossflow Safety Handbook*.

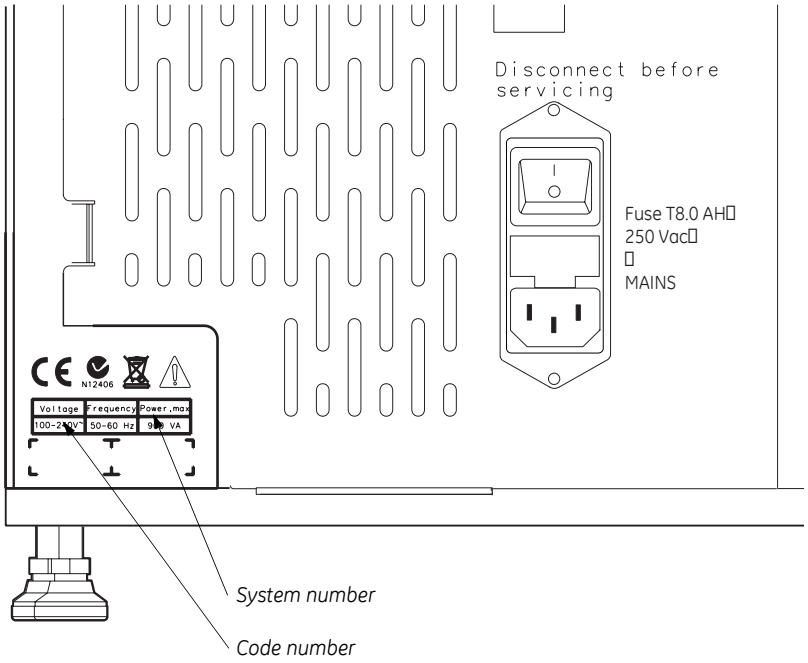


Fig 1-3. Layout of rating label.

1.4 Operating principles

This section gives an introduction to the function of the ÄKTAcrossflow system. ÄKTAcrossflow contains all the fluid handling components required to perform delivery of process fluids, filtration, and in-line monitoring. The fluid handling components are located on the front panel of the ÄKTAcrossflow instrument unit.

1.4.1 Liquid flow path

A schematic flow scheme for the ÄKTAcrossflow system is shown in Fig 1-4 below. The flow scheme shows an overview of the filtration system with transfer, recirculation (feed line and retentate line), and permeate lines.

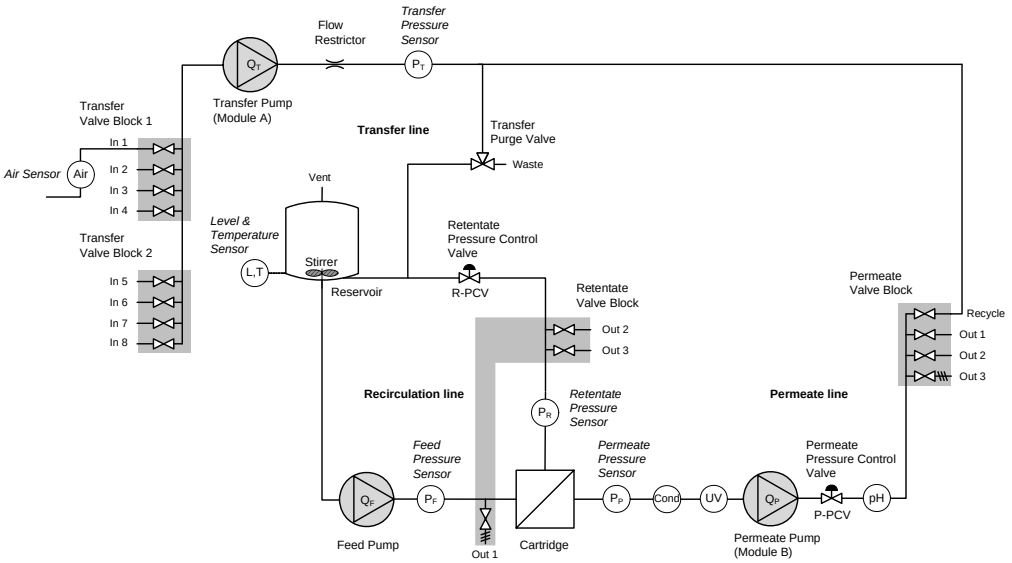


Fig 1-4. The liquid flow path of ÄKTAcrossflow.

Transfer line

The transfer line feeds sample or filtration buffer via the transfer pump to the reservoir.

Recirculation line (feed line and retentate line)

The feed line transfers the liquid via the feed pump from the reservoir to the CFF membrane. The liquid and components not passing the CFF membrane flow into the retentate line.

Permeate line

The permeate line transfers the liquid passing the CFF membrane via the permeate pump.

1.4.2 Ultrafiltration (UF)

Protein concentration
Workflow, see Fig 1-4

1 Filling of reservoir via inlet valve T-VB-In, transfer pump and transfer purge valve.

2 Filtration process.

3 Removal of protein concentrate via outlet valve R-VB-Out.

4 Removal of permeate via outlet valve P-VB-Out.

Protein diafiltration (DF)
Workflow, see Fig 1-4

1 Introducing buffer via inlet valve T-VB-In, transfer pump and transfer purge valve in continuous fed-batch mode.

2 Processing.

3 Product removal via outlet valve R-VB-Out.

1.4.3 Microfiltration (MF)

MF is used for cell harvest or clarification:

Workflow, see Fig 1-4:

1 Filling of reservoir via inlet valve T-VB-In, transfer pump and transfer purge valve.

2 Filtration process.

3 Product removal via outlet valve R-VB-Out, or clarified protein solution removal via outlet valve P-VB-Out.

1.4.4 Process optimization in 'total recycle mode'

Workflow, see Fig 1-4:

1 Filling of reservoir via inlet valve T-VB-In, transfer pump and transfer purge valve.

2 Process optimization (i.e. TMP scouting) with recycling of permeate into reservoir via permeate outlet valve P-VB-Recycle.

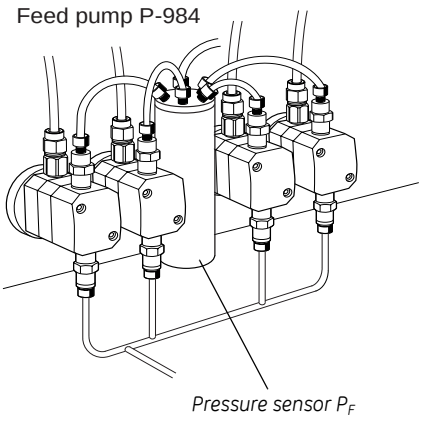
3 Removal of retentate via R-VB-Out.

1.5 Liquid delivery

1.5.1 Pumps

P-984

The feed pump, P-984, is a high-performance laboratory pump producing an accurately controlled liquid flow. It is designed for constant pulse-free inlet and outlet flow. The feed pump consists of four pump heads.



To prevent any deposition of salts from aqueous buffers and other organic compounds on the pistons, and to prolong the life of the seals, the pump has a piston rinsing system. The rinsing system tubing is connected to the rearmost holes on the pump heads.

The pump heads are equipped with check valves at the system flow inlet and outlet, and at the rinsing flow outlet.

The feed pump has an operating flow rate range up to 600 ml/min and a maximum allowed pressure of 5.2 bar.

P-982

Pump P-982 is identical with the P-984 pump except for the following:

1 Module A (two pump heads) is the transfer pump.

- The operating flow rate range is limited to 200 ml/min, and the pump is controlled to yield a constant pulse-free flow on the outlet.
- A pressure sensor (P_T) is connected to the transfer pump.

2 Module B (two pump heads) is the permeate pump.

- The operating flow rate range is limited to 200 ml/min, and the pump is controlled to yield a constant pulse-free flow on the inlet.

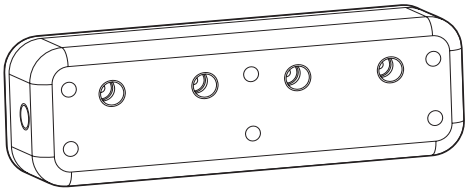
1.5.2 Valves

The liquid flow in the ÄKTAcrossflow system is controlled by valves of different functionality:

- Three membrane valve blocks comprising multiple inlets/outlets with open/close functionality
- One rocker valve block comprising multiple inlets/outlets with open/close functionality
- One 2-way switch valve
- Two pressure control valves for adjusting the pressure upstream of the valve

Membrane valve blocks

Each valve block comprises three or four stepper-motor actuated membrane valves with open/close functionality.



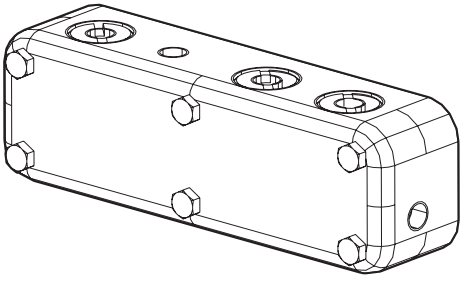
A valve block consists of a connection block containing the ports and the membranes. A mechanical housing containing the stepper-motors, cams and actuating pistons.

There are three membrane valve blocks in the flow path:

- Inlet valves T-VB-In: 1–4
- Inlet valves T-VB-In: 5–8
- Outlet valves P-VB-Out: recycle, 1, 2, 3 (pressure relief valve)

Rocker valve block

The valve block comprises three stepper-motor actuated diaphragm open/close valves. The diaphragm valve type comprises a membrane coated rocker.



The rocker closes against the flow through the inlet port

with the closing force controlled by the stepper-motor.

- Outlet valves R-VB-Out: 1 (pressure relief valve), 2, 3

One of the outlet valves, R-VB-Out 1, is used as pressure relief valve with the opening pressure 7 bar (102 psi).

WARNING! The pressure relief valves R-VB-Out 1 and P-VB-Out 3 must not be plugged.

2-way transfer purge valve

The 2-way switch valve is of diaphragm type and comprises a membrane coated rocker.

The transfer purge valve directs the liquid flow either from transfer line or permeate recycle towards the reservoir (default) or waste.

Pressure modulating/control valves R-PCV and P-PCV

The pressure control valves enable a throttling of the liquid flow in order to raise the pressure upstream of the valve.

- **Retentate control valve (R-PCV)**

  The retentate control valve R-PCV is used to accurately control the retentate pressure over the pressure range 0.1-5.2 bar. Hereby, the TMP can be adjusted, for example.

- **Permeate control valve (P-PCV)**

  The main task of the permeate control valve P-PCV is to modulate the pressure downstream the permeate pump in order to guarantee accuracy in the permeate flow rate by ensuring correct operation of the pump check valves.

Flow restrictor in transfer line

A flow restrictor is positioned downstream of the transfer pump in order to ensure a proper operation of the check valves at the pump heads, and thus accuracy in the transfer flow rate.

1.5.3 Reservoirs

The reservoir holds the liquid/sample to be processed. It provides a gentle, but efficient mixing of the process liquid with returning retentate as well as liquid added via the transfer line. Permeate may be recycled into the reservoir for achieving steady-state conditions during process development studies.

The reservoirs are equipped with a float to prevent vortex formation and foaming so that operation at lowest recirculation volume is facilitated at high flow rate.

There are two reservoir sizes:

- 350 ml (375 ml without float), mainly intended for UF/DF processes
- 1100 ml (1200 ml without float), mainly intended for MF processes

The reservoirs are mounted on the reservoir base, which comprises a motor unit for a magnetic stirrer. The stirrer can be used with both reservoirs to improve mixing characteristics.

1.5.4 CFF cassettes/cartridges

The CFF cassette/cartridge is the unit that encapsulates the filtration membrane.

Flat sheet membrane cassettes

There are two main sizes of flat sheet cassettes intended for UF/DF processes:

- 50 cm^2 membrane area, for typical feed flow rates of 25 to 40 ml/min – **Kvick™ Start**
- 100 cm^2 membrane area, for typical feed flow rates of 60 to 80 ml/min – **Kvick Lab Packet**

Hollow fiber membrane cartridges

There are two main sizes of hollow fiber cartridges intended for UF/DF processes:

- 50 cm^2 membrane area with a fiber length of 30 cm for feed flow rates of 24 to 200 ml/min
- 40 cm^2 membrane area with a fiber length of 60 cm for feed flow rates of 10 to 85 ml/min

The hollow fiber cartridge size intended for MF processes:

- 50 cm^2 membrane area with a fiber length of 30 cm for feed flow rates of 70 to 560 ml/min

1.5.5 Detectors and monitors

ÄKTAcrossflow is equipped with detectors for continuous in-line measurement of pressure, temperature, pH, conductivity and UV absorbance. The detectors provide accurate and reliable monitoring.

The flow cells for UV, conductivity and pH in the permeate line are connected close together, which minimizes volume and time delay between the detectors. The flow cells are easily accessible from the front panel to facilitate maintenance.

Pressure measurement

The pressure in the flow path is continuously measured by five pressure sensors:

- Pressure sensor P_T, located upstream from the reservoir.
- Pressure sensor P_F, located close to the CFF cassette/cartridge in the feed line.
- Pressure sensor P_R, located close to the CFF cassette/cartridge in the retentate line.
- Pressure sensor P_P, located close to the CFF cassette/cartridge in the permeate line.
- Reservoir level sensor, located in the reservoir bottom end plate.

Temperature measurement

- A temperature sensor, Temp, is integrated with the reservoir level sensor, and allows for continuous measurement of the liquid feed to the CFF cassette/cartridge.
- A second temperature sensor is integrated with the conductivity cell, and is used when calibrating the cell, see section 2.3.3.

pH measurement

The pH electrode is positioned downstream of the pressure control valve P-PCV.

The pH electrode is in continuous contact with the liquid in the permeate line, and can be used for the monitoring of the buffer exchange during diafiltration, for example. The pH monitor provides pH measurement in the range 1–14 (2-12 within specification).

Conductivity measurement

The conductivity cell is placed downstream from the permeate pressure sensor P_P in the permeate line.

The conductivity cell can be used for monitoring of the buffer exchange during diafiltration. The measurement range is 1 µS/cm to 250 mS/cm.

UV absorbance measurement

The UV cell is placed after the conductivity cell in the permeate line.

The cell is used for measuring the UV absorbance of the permeate. This information is useful to ensure protein rejection during ultrafiltration/ diafiltration steps, but also to monitor applications in cell processing. In its standard configuration, the detector features a single wavelength of either 254 or 280 nm. Filters to accommodate other wavelengths are optional.

Sample inlet air sensor

The air sensor in the flow path for the sample inlet ensures that the maximum volume of external feed can be transferred into the system without any risk for introducing air into the transfer line.

1.5.6 Tubing and connectors

When the ÄKTAcrossflow system is delivered, not all internal tubing is connected, refer also to section *5.1.7 – System flow path*. Some of the connection points on the unit are plugged. Remove the plugs and connect the hoses.

The tubings have an inner and outer diameter (i.d. and o.d.) of

- 1.7 mm and 3.0 mm respectively for PVDF tubing
- 2.9 mm and 4.76 mm (3/16") respectively for ETFE tubing

The tubes are pre-flanged and have UNF 5/16" male connectors with ethylenepropylenerubber (EPDM) O-rings for proper sealing and sanitizability.

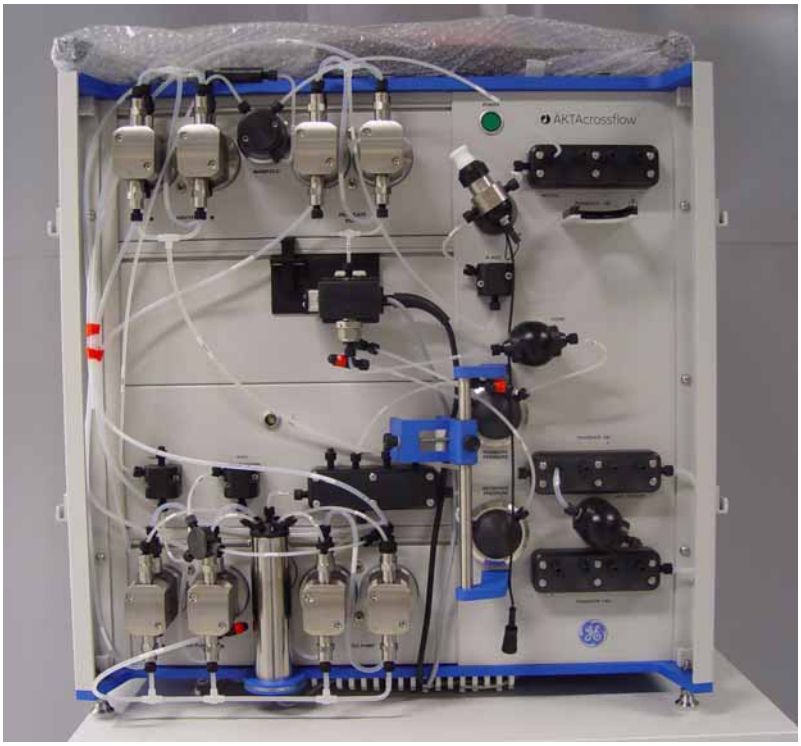


Fig 1-5. Tube connections on delivery.

Factory tubing connections shown in Fig 1-5. This is how the equipment should appear when it is unpacked. The permeate valve block and the transfer valve blocks are not fully connected. The tubing kits that are delivered with the equipment still have to be connected. Exactly how these are connected may vary from application to application but a basic connection example is shown in Fig 1-6.

Fig 1-7 shows an application with some small differences. The air sensor is connected to Transfer VB 2 instead of Transfer VB 1. Notice that the rails on the side of the unit are used to support containers.

Fig 1-6. Tube connections when the equipment is operational

Fig 1-7. Unit with bottles and resovoir.

1.5.7 Fraction collection (optional)

A separate fraction collector, Frac-920, can be connected to the outlet valves for collecting multiple fractions. Observe that when using Frac-920, the maximum allowed flow rate during fractionation is 100 ml/min.

For instructions on how to install Frac-920, refer to *ÄKTAcrossflow Installation Guide*.

1.6 Sanitization of the flow path

The fluid handling components in ÄKTAcrossflow have been designed to be compatible with recommended sanitization procedures. The Method Wizard includes a ready made method for sanitizing the system.

More information about sanitizing the system is found in the *ÄKTAcrossflow User Manual*.

1.7 Associated documentation

The following documentation is also included with ÄKTAcrossflow system:

The *ÄKTAcrossflow Installation Guide* provides instructions for installation of the system.

The *ÄKTAcrossflow User Manual* contains detailed operating instructions.

The *ÄKTAcrossflow Safety Handbook* contains safety information.

The *ÄKTAcrossflow Method Handbook* provides more detailed information on applications.

UNICORN control system package includes three manuals:

- *Getting Started*
- *User Reference Manual (2 pcs)*
- *Administration and Technical Manual*

Documentation of the ÄKTAcrossflow specific Evaluation module includes:

- *User Reference Manual – UNICORN 5.1 – Evaluation for cross-flow*
- Specific sections in *Online Help*

2 Basic operation

This chapter provides basic operating instructions for the ÄKTAcrossflow system. See *ÄKTAcrossflow User Manual* for more detailed instructions.

The chapter also contains instructions for calibrating the monitors.

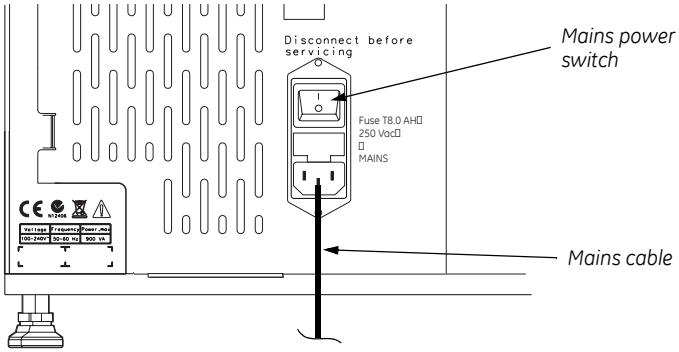
The start-up instructions in this chapter assume that the system has been correctly installed by personnel authorized by GE Healthcare.

WARNING! Do not operate the ÄKTAcrossflow system at pressures above the specified maximum pressure (5.2 bar).

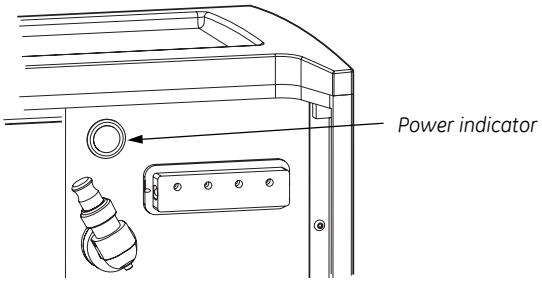
2.1 Starting the system

To start the ÄKTAcrossflow system:

1 Switch on the instrument with the mains power switch located on the rear panel.



- The **Power** indicator on the front panel flashes slowly until internal communication with the CU (Control Unit) is established.



- The **Power** indicator displays a constant green light when the internal communication with the CU is established.

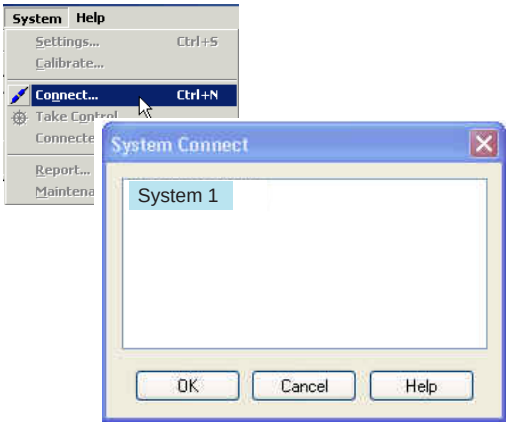
2 Switch on power to the PC and the monitor.

3 Start and log on to UNICORN by double-clicking on the icon on the Windows™ desktop.

4 Enter **User name** and **Password** and click **OK**.

Note: *When logging on for the first time, enter **default** as user name and password. For instructions on how to change user name and password, refer to ÄKTAcrossflow User Manual.*

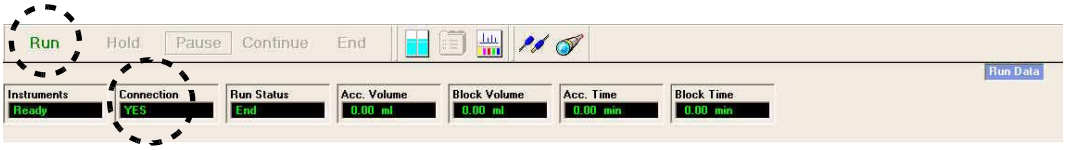
5 In the **System Control** module, select **System:Connect...** to connect UNICORN to the instrument unit.



6 Select the appropriate system name and click **OK**.

When the communication between UNICORN and the instrument unit is established:

- There is a constant green light on the **Power** indicator on the front panel.
- The green **Run** indicator in the status bar in UNICORN is lit.
- The **Connection** box shows **Yes**.



2.2 Set-up the instrument

2.2.1 Selecting reservoir

Before starting a filtration run, select reservoir size as follows:

- 350 ml for UF/DF processes
- 1100 ml for MF processes

CAUTION! When using the large reservoir and processing large volumes, a minimum working volume of 50 ml is recommended due to limitations in the accuracy of the retentate volume control. See Table 2-7 for details.

To change reservoir, follow the instructions below:

1 Switch off the system with the mains power switch.

2 Disconnect the inlet and outlet tubing.

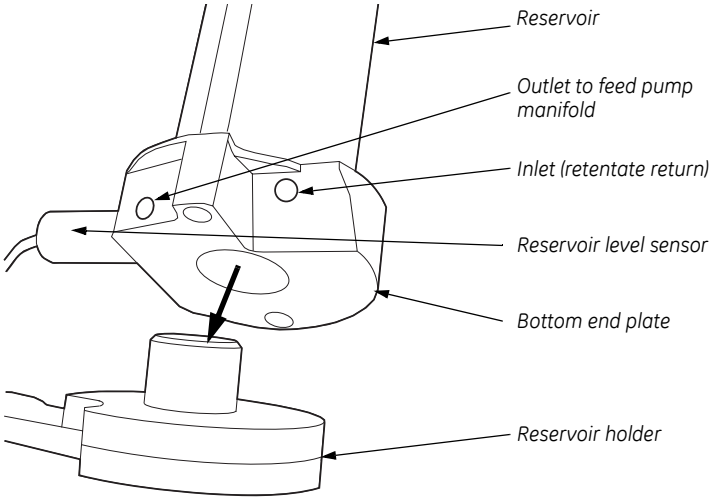
3 Disconnect the reservoir level sensor cable from the front panel.

4 Lift and remove the reservoir.

5 Disconnect the level sensor and mount it to the alternative reservoir.

CAUTION! The reservoir level sensor is highly sensitive. Be careful not to damage the sensor.

6 Mount the alternative reservoir, see figure below.



Note: *When using the large reservoir (1100 ml) the reservoir level sensor cannot be installed at a right angle to the front panel. The reservoir must be rotated to accommodate the level sensor.*

7 Connect the level sensor´s cable to the instrument´s front panel.

8 Connect the inlet and outlet tubing.

2.2.2 Configuration of tubing kits for high and low flow applications

As the ÄKTAcrossflow system offers a very broad range of flow rates, it is supplied with two tubing kits for the recirculation line to accommodate for applications and filters run at low and high flow rates as follows:

- Tubing with an inner diameter of 1.7 mm (Small) for low flow rate applications (typically < 80 ml/min feed flow rate)
- Tubing with an inner diameter of 2.9 mm (Large) for high flow rate applications (typically > 80 ml/min feed flow rate)

The system holdup volume and thus the working volume is minimized when using tubing with the small diameter.

Note: *The working volume is reservoir volume + system holdup volume + cassette/cartridge holdup volume.*

Recommended combinations of filters and tubing diameters are listed in Table 2-1

Filter cassette/cartridge	Application	Recommended tubing
Flat sheet, 50 cm^2	UF/DF	S = i.d. 1.7 mm
Flat sheet, > 50 cm^2	UF/DF	L = i.d. 2.9 mm, small i.d. tubing may be applicable depending on application
Hollow fiber, Start AXH	UF/DF	S = i.d. 1.7 mm
Hollow fiber, Start AXM	UF/DF	S = i.d. 1.7 mm, large i.d. tubing may be applicable for high flow/ high viscosity
Hollow fiber, Start AXM	MF	L = i.d. 2.9 mm

Table 2-1. Recommended combinations of filters and tubing diameters.

In order to compensate for different filter geometries and minimize holdup volume, the ÄKTAcrossflow system delivers tubing of different lengths with the cassette/cartridges.

Tubing kits

The tubing kits consist of the following tubing, see also Table 2-2 and Table 2-5 :

Small tubing i.d. 1.7 mm:

- Feed line: F1S, F2S, F3S, F4S
- Retentate line: R1S, R2S, R3S, R4S
- Permeate line: P1S

Large tubing i.d. 2.9 mm:

- Feed line: F1L, F2L, F3L, F4L
- Retentate line: R1L, R2L, R3L, R4L, R5L
- Permeate line: P1L

2.2.3 Kvick Start cassettes, cassette manifold and Kvick Lab Packet

WARNING! Hazardous chemicals. The cassette and cassette bag contain an aqueous solution containing up to 0.1–0.2 N NaOH and 20–22% (w/v) glycerin. When opening the cassette bag, follow the standard procedures for handling aqueous NaOH, including the use of safety glasses, safety gloves, and protective lab coat.

Preparing the cassette for use

To avoid unintentional spilling, hold the cassette package upright over a sink and trim the top of the cassette bag with a pair of scissors. Drain and dispose of excess storage solution in accordance with environmental regulations.

Remove silicone stoppers (or luer caps) from the ports, and allow any excess storage solution to drain from the cassette.

To avoid inadvertent contact with the storage solution after the cassette is removed from the bag, rinse the outside surface of the cassette with distilled water.

If you allow an ultrafiltration cassette to dry out, the membrane will be damaged. Therefore, do not store the cassette without re-wetting it with an approved storage solution.

For instructions on cleaning a new or a used flat sheet membrane cassette and system prior to a filtration run, refer to *ÄKTAcrossflow User Manual*, *Chapter 5 – Creating Preproduct methods using the Method Wizard*.

Connecting the Kvick Start cassette

Install the cassette on the instrument unit. Carefully attach the cassette in the holder by tightening the locking screw, see Fig 2-8 below.

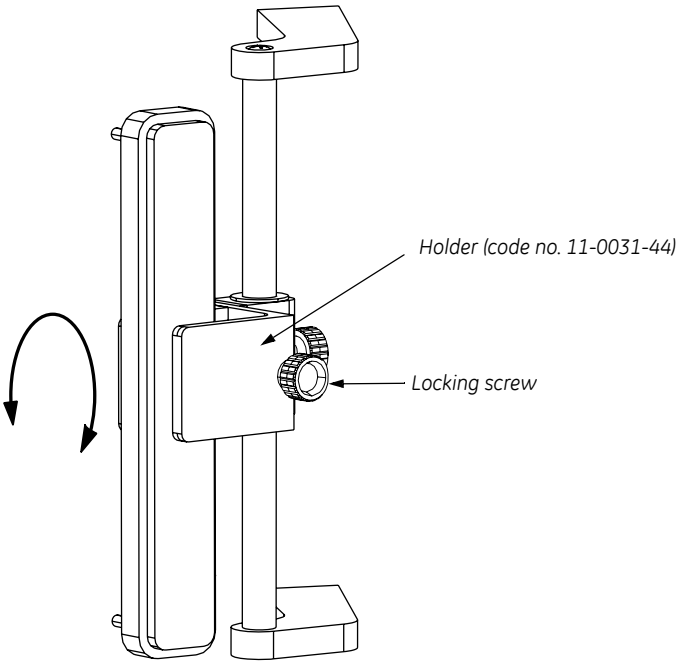


Fig 2-8. Holder for flat sheet membrane cassette.

The holder (see figure above) is spring-loaded, and can be rotated 360° without loosening any screws. It has fixed positions at each 90°, i.e. vertical or horizontal position.

The holder allows cassettes with thickness from 17 to 40 mm.

Connecting tubing to Kvick Start cassette

Connect the cassette to the retentate, permeate and feed lines, see Fig 2-9 below. To minimize holdup and working volume, the recommended tubing length for use with 50 cm^2 flat sheet cassettes is listed in Table 2-2 . For selection of tubing diameter, see Table 2-1 .

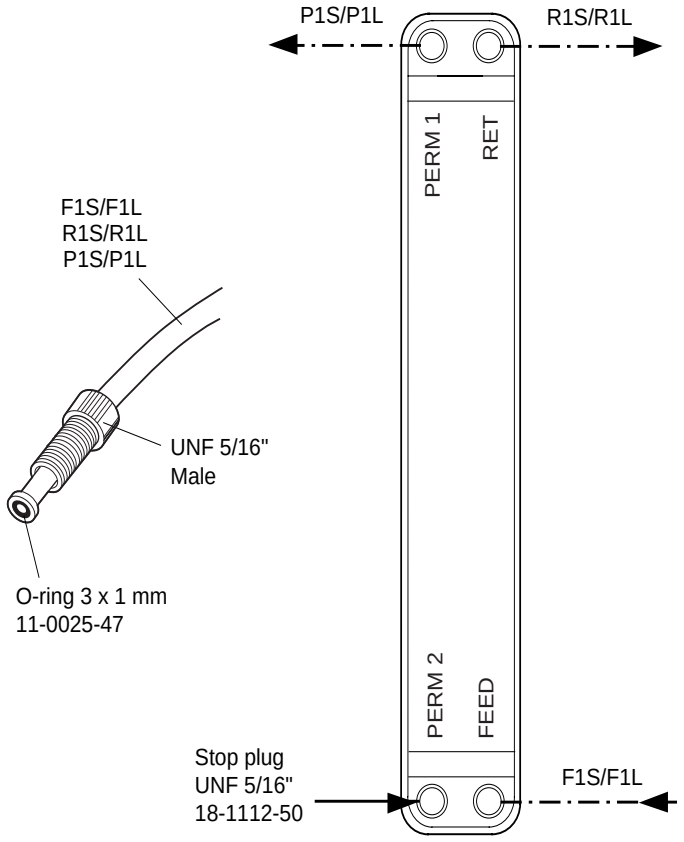


Fig 2-9. Flat sheet membrane cassette - Kvick Start.

Tubing	Length [mm]	O.d. [mm]	I.d. [mm]	Volume [ml]	Material	Location From	Location To
F1S	200	3	1.7	0.45	PVDF	Valve block R-VB	Cassette, feed inlet
F1L	200	4.76 (3/16")	2.9	1.32	ETFE		
R1S	300	3	1.7	0.68	PVDF	Cassette (RET), retentate outlet	Sensor P_R, inlet
R1L	300	4.76 (3/16")	2.9	1.98	ETFE		
P1S	155	3	1.7	0.35	PVDF	Cassette (PERM1), permeate outlet	Sensor P_P, inlet
P1L	150	4.76 (3/16")	2.9	0.99	ETFE		

Table 2-2. Recommended tubing for flat sheet membrane cassettes.

Connecting tubing to the cassette manifold kit

Connect the cassette manifolds to the cassettes, and to the retentate, permeate and feed lines, see Fig 2-10 below. To minimize holdup and working volume, the recommended tubing length for use with 3 × 50 cm^2 flat sheet cassettes are listed in Table 2-3 . For selection of tubing diameter, see Table 2-1 .

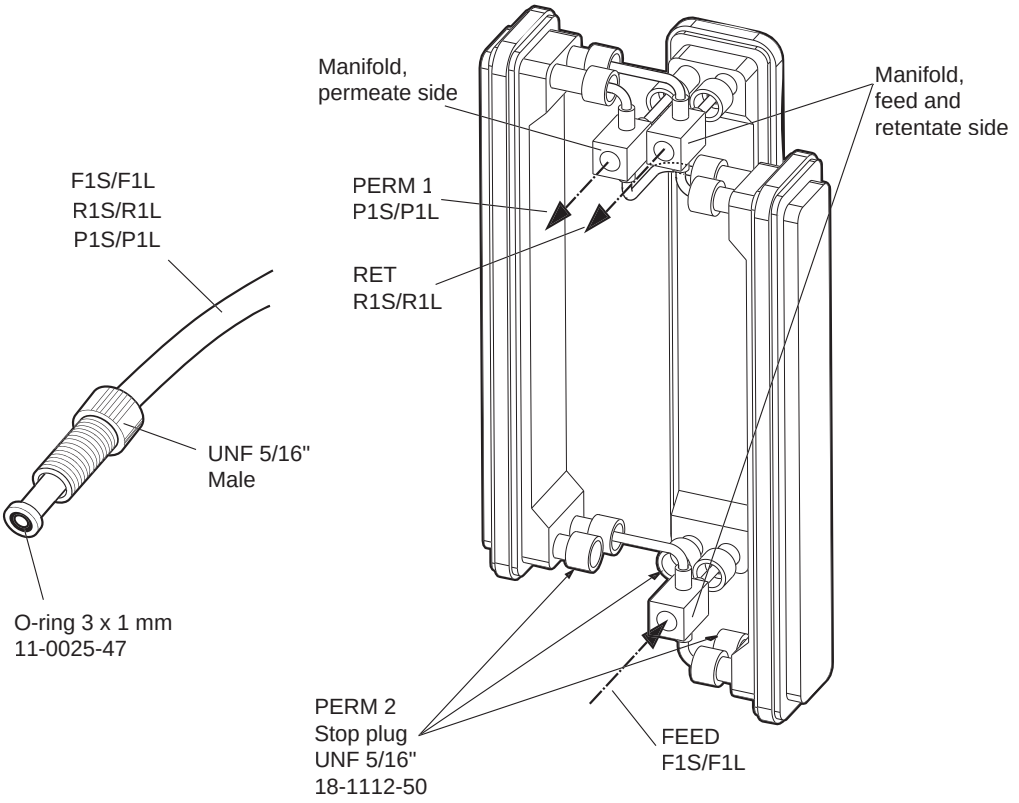


Fig 2-10. Cassette manifolds.

Tubing	Length [mm]	O.d. [mm]	I.d. [mm]	Volume [ml]	Material	Location From	Location To
F1S	200	3	1.7	0.45	PVDF	Valve block R-VB	Cassette, feed inlet
F1L	200	4.76 (3/16")	2.9	1.32	ETFE		
R1S	300	3	1.7	0.68	PVDF	Cassette (RET) retentate outlet	Sensor P_R, inlet
R1L	300	4.76 (3/16")	2.9	1.98	ETFE		
P1S	155	3	1.7	0.35	PVDF	Cassette (PERM1) permeate outlet	Sensor P_P, inlet
P1L	150	4.76 (3/16")	2.9	0.99	ETFE		

Table 2-3. Recommended tubing for cassette manifold kit.

Connecting the cassette manifold kit

Install the cassette manifold (see Fig 2-10 below) to the instrument unit by using the same holder as for a single cassette, see Fig 2-8. Carefully attach one of the three cassettes in the holder by tightening the locking screw, see Fig 2-8.

When using the cassette manifold kit (11-0031-53) the retentate holdup volume increases by 0.76 ml (2 × 0.38 ml at the feed and retentate manifolds). This volume needs to be considered as extra tubing volume when programming methods, i.e. when using the Method Wizard. The increase of holdup volume in the permeate line due to the manifold at the permeate outlet is 0.43 ml.

Connecting the Kvick Lab Packet

Install the Kvick Lab Packet into the Kvick Lab Packet Holder according to the instructions supplied with that holder. Install the Packet Holder to the instrument by using the same instrument holder as mentioned above for the Kvick Start installation, see Fig 2-8.

Connecting tubing to Kvick Lab Packet

Connect the Kvick Lab Packet to the retentate, permeate and feed lines, see Fig 2-11 below. To minimize holdup and working volume, the recommended tubing length for use with 100 cm^2 flat sheet membranes are listed in Table 2-4 .

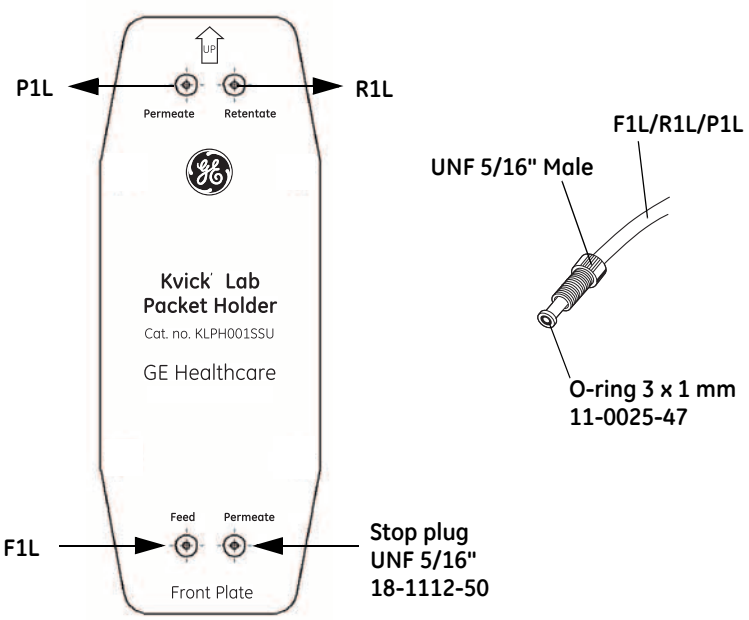


Fig 2-11. Kvick Lab Packet Holder.

Tubing	Length [mm]	O.d. [mm]	I.d. [mm]	Volume [ml]	Material	Location From	Location To
F1S	200	3	1.7	0.45	PVDF	Valve block R-VB	Kvick Lab Packet, feed inlet
F1L	200	4.76 (3/16")	2.9	1.32	ETFE		
R1S	300	3	1.7	0.68	PVDF	Kvick Lab Packet, retentate outlet	Sensor P_R, inlet
R1L	300	4.76 (3/16")	2.9	1.98	ETFE		
P1S	155	3	1.7	0.35	PVDF	Kvick Lab Packet, permeate outlet	Sensor P_P, inlet
P1L	150	4.76 (3/16")	2.9	0.99	ETFE		

Table 2-4. Recommended tubing for Kvick Lab Packet.

2.2.4 Hollow fiber membrane cartridges

Preparing the cartridge for use

- **ULTRAFILTRATION**

  Removal of glycerol preservative

  UF membrane cartridges are pretreated with an isopropanol/glycerol solution within the pore structure to prevent drying of the membrane. This mixture enhances wetting but may cause the fibers to appear wavy. Trace amounts of isopropanol may remain when the cartridges are shipped.

  The glycerol must be thoroughly rinsed from the cartridge prior to use. In addition to preventing drying, the glycerol minimizes entrained air within the pore structure of the membrane wall which may become “locked-in” reducing permeability until the air has been displaced by liquid.

- **MICROFILTRATION**

  Although MF membrane cartridges are shipped dry, without preservative solutions, it is prudent to rinse cartridges before first process exposure or heat sterilization.

For instructions on cleaning a hollow fiber membrane cartridge and system prior to a filtration run, refer to *ÄKTAcrossflow User Manual*, *Chapter 5 – Creating Preproduct methods using the Method Wizard*.

Connecting the cartridge

Install the cartridge on the instrument unit as follows:

1 Mount the block to the holder, see Fig 2-12 below.

Note: *The block is delivered with the Accessory box.*

2 Carefully attach the cartridge in the holder by tightening the locking screw, see Fig 2-12 below.

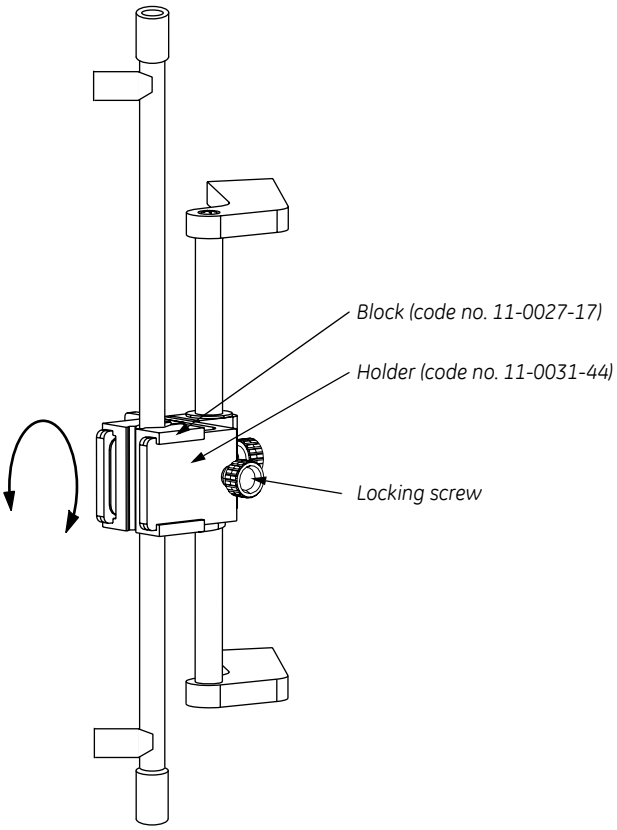


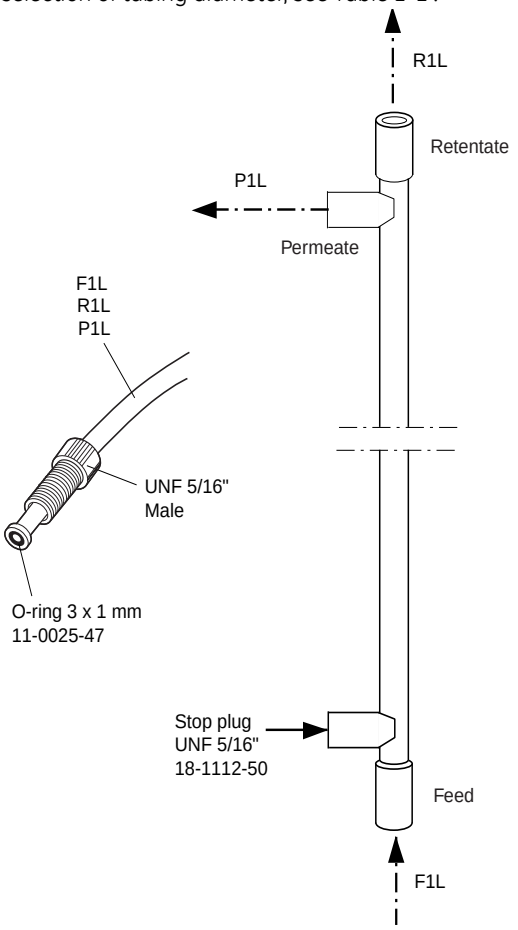
Fig 2-12. Holder for hollow fiber membrane cartridge.

The holder (see figure above) is spring-loaded, and can be rotated 360° without loosening any screws. It has fixed positions separated by 90°, i.e. vertical or horizontal position.

The holder allows cartridge diameters from 3 to 23 mm.

Connecting tubing to cartridge

Connect the cartridge to the retentate, permeate and feed lines, see figure below. To minimize holdup and working volume, the recommended tubing length for use with the Start AXM hollow fiber cartridge is listed in Table 2-5 . For selection of tubing diameter, see Table 2-1 .

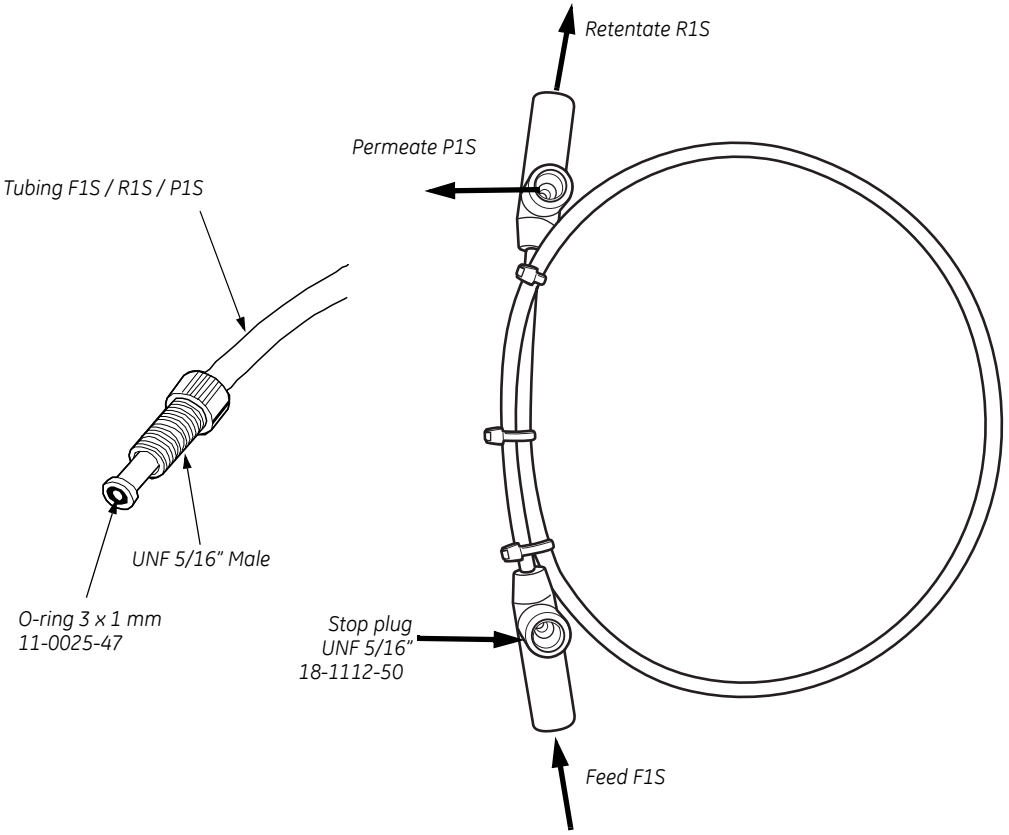


Tubing	Length [mm]	O.d. [mm]	I.d. [mm]	Volume [ml]	Material	Location From	Location To
F1S	300	3	1.7	0.68	PVDF	Valve block R-VB	Cartridge, feed inlet
F1L	300	4.76 (3/16")	2.9	1.98	ETFE		
R1S	200	3	1.7	0.45	PVDF	Cartridge, retentate outlet	Sensor P_R, inlet
R1L	200	4.76 (3/16")	2.9	1.32	ETFE		
P1S	155	3	1.7	0.35	PVDF	Cartridge, permeate outlet	Sensor P_P, inlet
P1L	150	4.76 (3/16")	2.9	0.99	ETFE		

Table 2-5. Recommended tubing for Start AXM hollow fiber membrane cartridges, see also Table 2-1 .

Connecting the Start AXH cartridge

The Start AXH cartridge can be installed by connecting it to the retentate, permeate and feed lines, see figure below and Table 2-6 . There is no need for a holder.



Tubing	Length [mm]	O.d. [mm]	I.d. [mm]	Volume [ml]	Material	Location From	Location To
F1S	200	3	1.7	0.45	PVDF	Valve block R-VB	Cartridge, feed inlet
R1S	200	3	1.7	0.45	PVDF	Cartridge, retentate outlet	Sensor P_R, inlet
P1S	155	3	1.7	0.35	PVDF	Cartridge, permeate outlet	Sensor P_P, inlet

Table 2-6. Recommended tubing for Start AXH hollow fiber membrane cartridges.

2.2.5 Creating a method

Refer to *ÄKTAcrossflow User Manual*.

2.2.6 Preparing the system

Before starting a method, check the following:

- The inlet tubings are immersed in or connected to the correct bottles, refer to section 5.1.3.
- There is sufficient buffer available.
- The waste bottles are not full and will accept the volume diverted to them during the run, refer to section 5.1.3.
- The inlet tubing and the pumps are primed by using a Method Wizard created preproduct method, refer to *ÄKTAcrossflow User Manual*.
- The pH electrode is calibrated (if required). Refer to section 2.3.2 Calibrating the pH electrode.
- The correct reservoir has been installed.
- The correct CFF cassette/cartridge has been installed and rinsed with process buffer by using a Method Wizard created preproduct method, refer to *ÄKTAcrossflow User Manual*.

  Note: *For instructions on how to select CFF cassette/cartridge in UNICORN, refer to ÄKTAcrossflow User Manual.*

- The outlet tubings are immersed in the correct bottles.

WARNING! OVERPRESSURE. Never block the outlet tubing and the pressure relief valves outlet with, for example, stop plugs, since this will create overpressure and may result in injury.

- The fans should operate, producing a cooling air flow that exits at the right-hand side of the instrument.

Note: *See ÄKTAcrossflow User Manual for more detailed instructions before starting a run.*

2.2.7 Running a method

Refer to *ÄKTAcrossflow User Manual*.

2.2.8 After the run

Clean the system according to the instructions in section *3.2.1 Cleaning the system*.

2.3 Calibration

The monitors in the ÄKTAcrossflow system need to be calibrated regularly to ensure correct results. This section shows the type of calibrations that can be done, how to perform the calibrations and how often. The calibrations are performed from UNICORN by selecting **System:Calibrate...** in the **System Control** module.

Component	How often
Pressure sensor P_T	Only when zero pressure-reading calibration is needed, see section 2.3.1.
pH electrode	Every day, see section 2.3.2.
Conductivity cell	
Temperature sensor	Must be performed when changing the cell.
Entering a new cell constant	Must be performed when changing the cell.
Cell constant	Only necessary when specific conductivity with high accuracy is measured. See section 2.3.3.
Reservoir level sensor	Prior to every run, see section 2.3.4.

2.3.1 Calibrating the pressure sensors

In pressure sensor P_T, the zero pressure-reading can be calibrated. The amplification in sensors P_T, P_F, P_R and P_P is already calibrated at the factory.

Calibrating pressure sensor P_T

To calibrate the zero pressure-reading:

1 In the **System Control** module, select **Manual:Transfer.**

2 Set the instruction **Transfer Purge Valve** to **Waste**. Click **Execute**.

3 Set the instruction **Transfer Valve Block 1** to **T-VB-In1**. Click **Execute**.

4 Immerse the tubing from valve **T-VB-In1** in distilled water.

5 Select **System:Calibrate.**

6 In the **Calibration** window, select **TrfPress**.

7 Click **Read value** when the pressure is stable. The zero pressure-reading is now calibrated.

8 Press **END** to finish calibration.

2.3.2 Calibrating the pH electrode

A good laboratory routine is to calibrate the pH electrode at least once a day, when the electrode is replaced or if the ambient temperature is changed. The pH electrode is calibrated using standard buffer solutions in a two point calibration. The two buffer solutions may have any pH value as long as the difference between them is at least 1 pH unit, and the expected pH during the run is within this interval.

Note: *The pH-calibration kit can be found in the Accessory box.*

Calibrating with the electrode outside the cell holder

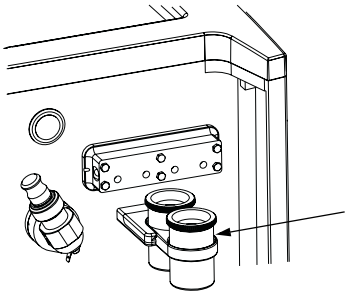
When calibrating the electrode out of the cell holder and changing from one buffer to another, rinse the electrode tip with distilled water and dab it carefully with a soft tissue to absorb the remaining water. Do NOT wipe the electrode as this may charge it and give unstable readings.

1 In the **System Control** module, select **System:Calibrate.**

2 Select **pH** from the **Monitor** pop-up menu in the **Calibration** window.

3 Prepare two reference buffer solutions, the first normally pH 7.0. The difference in pH value between them must be at least 1 pH unit. The expected pH value during the run should be within this interval.

4 Use the holder on the front panel for the reference buffer solution containers, see figure below.



5 Remove the pH electrode from the cell holder and immerse the electrode in the first reference solution.

Note: *To avoid leakage from the system after removing the pH electrode, replace it with the pH electrode dummy.*

6 Enter the known pH value of the solution in the **Reference value 1** field.

7 The pH reading is shown under **Measured value.** When the pH value has stabilized, click **Read value 1.**

8 Rinse the electrode tip with distilled water and then immerse the electrode in the second reference solution (e.g. pH 4.0 or 9.0).

9 Enter the known pH value of the second reference solution in the **Reference value 2** field.

10 When the pH value has stabilized, click **Read value 2.** The calibration is finished.

11 After the calibration, values are automatically entered into the **Asymmetry potential at pH7; mV** and **Calibrated electrode slope; %** fields.

A new electrode has a slope of typically 95–102% and an asymmetry potential within ±30 mV. As the electrode ages, the slope decreases and the asymmetry potential increases.

As a rule, when the **Asymmetry potential at pH7; mV** value is outside of ±60 mV and the **Calibrated electrode slope; %** value is lower than 80%, and no improvement can be achieved by cleaning, the electrode should be replaced.

An electrode is still usable at lower slopes and higher asymmetry potentials but the response will be slower and the accuracy diminished.

Before use, rinse the pH electrode using distilled water.

2.3.3 Calibrating the conductivity cell

Entering a new cell constant

After replacing the conductivity cell, the cell constant has to be set. The cell constant is shown on the packaging of the new cell.

1 In the ***System Control*** module, select ***System:Calibrate...*** and then ***Cond_Cell*** in the ***Monitor*** pop-up menu.

2 Enter the cell constant in the ***Reference value 1*** field.

3 Click ***Read value 1***. The new cell constant is updated. Click ***Close.***

Calibrating the temperature sensor

Calibration of the temperature sensor in the conductivity cell is only necessary when the cell is used in high accuracy measurements or if the cell is replaced.

1 Ensure that the conductivity cell together with a precision thermometer are not exposed to draft. Leave them for 15 minutes to let the temperature stabilize.

2 In the ***System Control*** module, select ***System:Calibrate...*** and choose ***Cond_Temp*** in the ***Monitor*** pop-up menu.

3 Read the temperature on the thermometer.

4 Enter the temperature in the ***Reference value 1*** field.

5 Click the ***Read value 1*** button.

Setting up conductivity temperature compensation

The conductivity of a buffer is temperature dependent. To relate conductivity to concentration and/or compare conductivity values, temperature compensation should be used. The compensation consists of a compensation factor together with a reference temperature. All conductivity values will then automatically be converted to the set reference temperature.

1 In the ***System Control*** module, select ***System:Settings...*** and click the ***Monitors*** radio button.

2 Choose the instruction ***CondTempComp.***

3 The factor is expressed in percentage increase of conductivity per °C increase in temperature. If the temperature compensation factor is unknown, a general approximate value of 2% can be set for many common salt buffers.

If no temperature compensation is needed, enter the value 0% in the ***CompFactor*** field.

4 Choose the instruction **CondRefTemp.**

5 Select the reference temperature to which the measured conductivity values will be converted (normally 20 or 25 °C).

Enter an appropriate temperature in the **RefTemp** field.

6 Click ***OK.***

Calibrating the cell constant

Normally it is not necessary to adjust the cell constant as the cell is pre-calibrated on delivery. Adjustment is only necessary when replacing the conductivity cell with a cell whose cell constant is unknown, or when changing strategy. We also recommend that the conductivity cell is recalibrated after cleaning.

Note: *The conductivity temperature compensation must not be used when adjusting the cell constant. Set the compensation factor to 0 (see section Setting up conductivity temperature compensation).*
The temperature sensor must be calibrated before adjusting the cell constant (see section Calibrating the temperature sensor).

1 Prepare a calibration solution of 1.00 M NaCl, 58.44 g/l. Let the solution reach room temperature. This is important for exact measurements.

2 Fill the cell completely with the calibration solution by pumping at least 15 ml through the cell with a syringe.

3 When finished, wait for 15 minutes until the temperature is constant in the range 20–30 °C.

4 In the **System Control** module, select **System/Calibrate.** Select **Cond_Cal** in the **Monitor** pop-up menu.

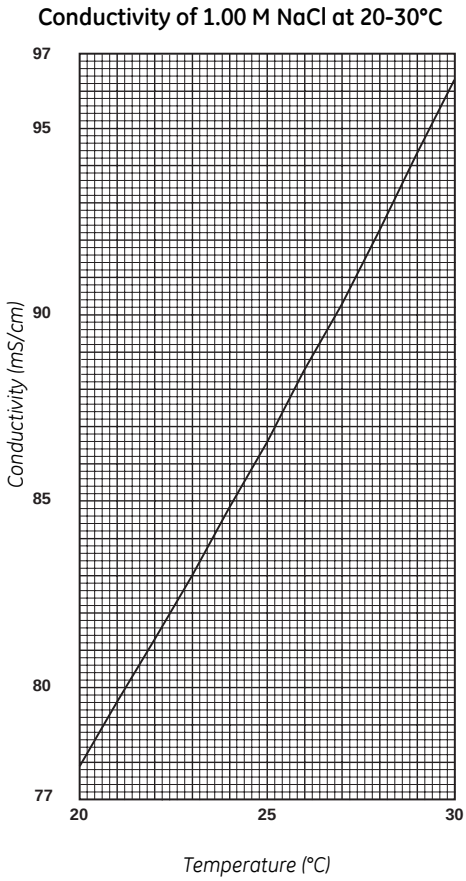
5 Read the conductivity value displayed under **Measured value** and compare it with the theoretical value from the graph opposite at the temperature of the calibration solution.

If the displayed value and the theoretical value correspond, no further action is required.

If the values differ, proceed with step 6 and 7.

6 Enter the theoretical conductivity value according to the graph in the **Reference value 1** field.

7 Click the **Read value 1** button. The new cell constant is automatically calculated and updated.



2.3.4 Calibrating the reservoir level sensor

The reservoir level sensor can be calibrated using the Method Wizard or manually.

However it is recommended that the Method Wizard is used to calibrate the level sensor because it reduces the risk of error and is also more convenient since all calibration steps are performed automatically.

Note: *When calibrating the level sensor the liquid used must be at the ambient temperature.*

To calibrate the level sensor using the Method Wizard

1 Open the reservoir lid to allow air to flow freely into the reservoir.

2 In System Control select **File/Instant Run**

3 In the Method Wizard Dialog select **Calibrate Level Sensor**. Follow the instructions and then press **Run**.

4 Start notes and Method Information are displayed. Press **Next** after each page.

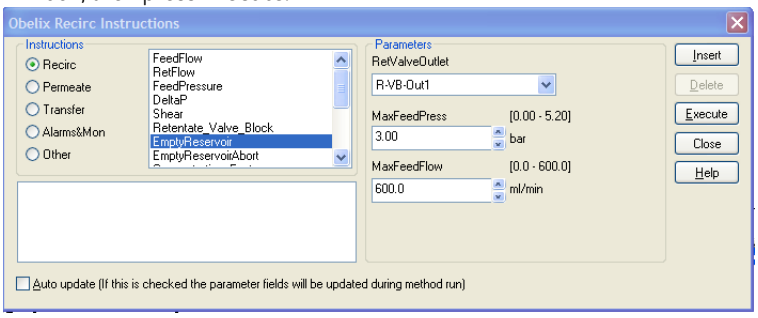
5 Start the method by pressing **START**.

6 Wait until the calibration is finished (approx. 5 minutes).

To calibrate the level sensor manually.

1 Empty the reservoir manually as follows:

- Open the reservoir lid to allow air to flow freely into the reservoir.
- In the Recirc Instructions dialog, select **Recirc:EmptyReservoir:R-VB-Out1.** Enter **3** in the **MaxFeedPress** box and **600** in the **MaxFeedFlow** box, then press **Execute**.

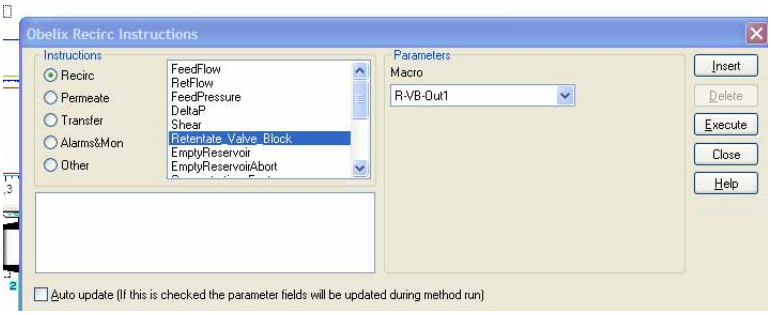


- Wait until the reservoir is emptied.

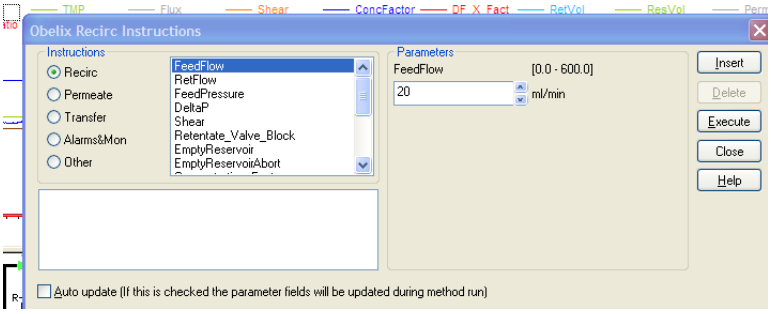
Note: *The **EmptyReservoir** instruction empties the reservoir but not the*

small cavity in the bottom of it. This cavity must also be emptied before calibration. How this is done is described below.

- In the Recirc Instructions dialog, select **Recirc:Retentate_Valve_Block: R-VB-Out1,** then press **Execute.**



- In the Recirc Instructions dialog, select **Recirc:FeedFlow.**



- In the **FeedFlow** box, select **20** ml/min, and then click **Execute.**
- Check that the cavity in the bottom of the reservoir is completely empty. Do not close the flow.

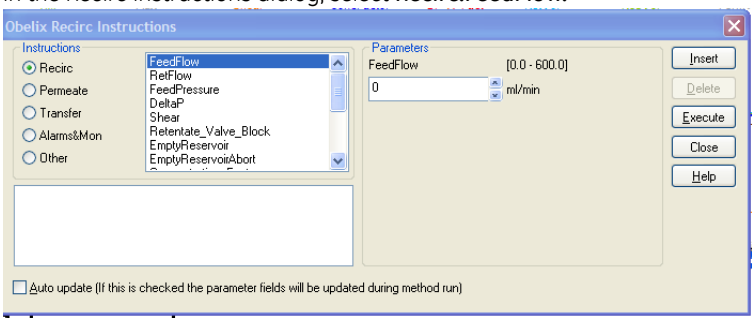
2 In the **System Control** module, select **System:Calibrate.** The **Calibration** dialog appears.

In the **Monitor** box, select **ZeroLS.** Click the **Start calibrate** button to reset the level sensor reading to ***0.***

The **Start calibrate** button will be disabled and the cursor will turn into an hourglass for a few seconds while the calibration is in progress.

CAUTION! The reservoir level sensor is highly sensitive. Do not insert any objects into the cavity in the bottom end plate of the reservoir since this may damage the level sensor.

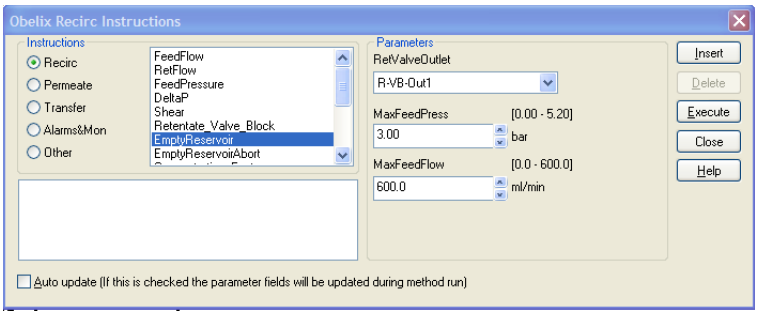
3 In the Recirc Instructions dialog, select **Recirc:FeedFlow.**



- Close the feed line by selecting **0** ml/min in the FeedFlow box, and then click **Execute.**
- Set **Retentate_Valve_Block** to **R-VB-recycle**
- Click **Close.**

4 Fill the reservoir with 50 ml of distilled water, manually or by using the transfer pump.

5 Empty the reservoir by selecting **Recirc:EmptyReservoir:R-VB-Out1,** and enter **3** in the **MaxFeedPress** box and **600** in the ***MaxFeedFlow*** box.



- Click **Execute.**
- Click **Close.**

2.3.5 Setting the retentate holdup volume

The retentate volume is the sum of retentate holdup volume and the liquid volume in the reservoir:

RetVol = RetentateHoldupVolume + ResVol

The reservoir volume in the ÄKTAcrossflow system is monitored and controlled by the reservoir level sensor, and pumped volumes reported by the pumps. In order to calculate the correct retentate volume, user-defined input on the retentate holdup volume is required. The retentate holdup volume is the sum of system holdup volume (in components and tubing) and the retentate volume in the filter:

RetentateHoldupVolume = system holdup volume + filter volume

The system holdup volume depends on the tubing configuration, see Table 2-7 .

Recirculation tubing kit	Feed tubing	Retentate tubing	Permeate tubing	System holdup volume* [ml]	Min. working volume** [ml]	
					350 ml Reservoir	1100 ml Reservoir
Small i.d. (1.7 mm)	F1S 200	R1S 200	P1S 155	18.2	24 (22.2)	40 (26.2)
Small i.d. (1.7 mm)	F1S 300	R1S 200	P1S 155	18.4	24 (22.4)	45 (26.4)
	F1S 200	R1S 300				
Large i.d. (2.9 mm)	F1L 200	R1L 300	P1L 150	25.8	32 (29.8)	50 (33.8)
	F1L 300	R1L 200				

* System holdup volumes do not account for filter volume:
RetentateHoldupVolume = system holdup volume + filter volume.

** Recommended min. working volume accounting for accuracy in control and measurement of retentate volume.
The figures in brackets state typical values for the lowest possible working volume (excluding filter volume).

Table 2-7. System holdup volume and recommended minimum working volume.

The retentate holdup volume **RetentateHoldupVolume** is defined as default value in the system settings. When executing methods, this figure will be overwritten as soon as the method provides a new figure for the **RetentateHoldupVolume**. Methods generated by the Method Wizard will automatically provide the correct retentate holdup volume via user input in the dialog of the Method Wizard.

If the retentate holdup volume cannot be determined theoretically, the retentate line (including filter) can be emptied by pumping air until it is completely filled with air. Then, a known amount of liquid (50 ml) can be added to the reservoir and recirculated at low feed flow such that all air is removed from the retentate line. Finally, the reservoir is emptied manually and the volume in the reservoir is determined. The retentate holdup volume equals the difference between the volume of added and recovered liquid.

2.4 Stop the pumps

To stop the pumps:

1 In the UNICORN status bar, click the ***Pause*** button.

2 Click the ***Continue*** button to restart the pumps.

It is also possible to stop the pumps in the **System Control** module in UNICORN. See *ÄKTAcrossflow User Manual* – Chapter *Performing crossflow runs manually*.

2.5 Shut down the system

To shut down the ÄKTAcrossflow system:

1 Close down the ÄKTAcrossflow UNICORN software by choosing **File/Exit** in the UNICORN manager module.

2 Switch off mains power on the rear panel of the instrument.

2.5.1 Restart procedure

To restart the ÄKTAcrossflow system, follow the start-up instructions in section 2.1.

3 Maintenance

Regular maintenance is important for safe and trouble-free operation of the ÄKTAcrossflow system. The user should perform daily and monthly maintenance.

This chapter provides instructions for user maintenance and for replacing spare parts.

Contact your GE Healthcare representative for more service information.

WARNING! NO SERVICEABLE PARTS INSIDE. Do not open covers. Service and planned maintenance should be performed by personnel authorized by GE Healthcare.

WARNING! When using hazardous chemicals, take all suitable protective measures, such as wearing protective glasses and gloves resistant to the chemicals used. Follow local regulations and instructions for safe operation and maintenance of the system.

WARNING! When using hazardous chemicals, make sure that the entire system has been flushed thoroughly with bacteriostatic solution, e.g. NaOH, and distilled water before service and maintenance.

WARNING! NaOH is corrosive and therefore dangerous to health. Avoid spillage and wear safety glasses, safety gloves and protective lab coat.

WARNING! If there is a risk that large volumes of spilt liquid might penetrate the casing of the instrument and come into contact with the electrical components, immediately switch off the system and contact an authorized service technician.

WARNING! Heavy object. The instrument unit weighs 70 kg. Use suitable lifting equipment when moving the system. Wear safety shoes. For lifting instructions, refer to *ÄKTAcrossflow Installation Guide*.

WARNING! The instrument has a high center of gravity. Due to the risk of tipping over, do not place the instrument close to the edge of the bench.

WARNING! The instrument has feet with low friction. To prevent the instrument from sliding, the bench surface must not be inclined.

WARNING! Remove liquid or dirt from the system surface using a cloth and, if necessary, a mild cleaning agent.

CAUTION! Only use spare parts supplied or specified by GE Healthcare.

3.1 User maintenance schedule

Table 3-8 lists the maintenance operations that should be performed by the user at regular intervals.

Interval	Action	Instructions/reference
Daily		
System	Clean the cover	See section 3.2.1.
	Inspect the system for liquid leakage	Check that tubing and connectors are not damaged. Replace if necessary.
	Wash the system flow path	Avoid leaving the system filled with buffer overnight. Wash the flow path with distilled water. If leaving the system for a few days, use 20% ethanol. Make sure that all tubing and flow paths used are rinsed. See section 3.2.1.
	Check fan operation	Check that cooling air flows through the system, exiting at the right-hand side of the instrument.

Interval	Action	Instructions/reference
Feed pump Transfer pump Permeate pump	Check for leakage	If there are signs of liquid leaking between a pump head and the system panel, or increased or decreased volume of rinsing solution, replace the piston assembly, glass tube, and/or O-rings in the pump head. See section 3.3.2.
	Remove air bubbles	When changing buffer, it is important to remove trapped air. Prime the pump (see section 3.4).
pH electrode	Calibrate the pH electrode	See section 2.3.2 Replace the pH electrode if necessary. See section 3.3.11.
Pump rinsing solution	Change rinsing solution	Use 10 mM NaOH in 20% ethanol as rinsing solution. If the volume of rinsing solution in the storage bottles has increased, it can be an indication of internal pump leakage. Replace the piston assembly, glass tube, and/or O-rings in the pump head according to section 3.3.2. If the volume of rinsing solution in the storage bottle has decreased significantly, check that the rinsing system connectors are mounted properly. If the rinsing system connectors are not leaking, the piston, glass tube, and/or O-rings might be damaged. Replace according to section 3.3.2.
Every 3rd month		
UV flow cell	Check UV lamp run time	See section 3.2.4

Interval	Action	Instructions/reference
Every 6th month		
UV flow cell (or when required)	Clean the UV flow cell	Clean the cell to ensure proper UV monitoring. See section 3.2.4.
Conductivity cell (or when required)	Clean the conductivity cell	See section 3.2.6
Every year		
Reservoir	Replace the stirrer bar	
When required		
Feed pump Transfer pump Permeate pump	Replace piston	See section 3.3.2
	Replace glass tube	See section 3.3.2
	Replace O-rings	See section 3.3.2
	Clean or replace the inlet and outlet check valves. Clean the rinsing system check valve.	See section 3.2.2 and 3.3.2
pH electrode	Clean the pH electrode	See section 3.2.5
Valve blocks	Replace the membranes	See section 3.3.3
	Replace the rocker	See section 3.3.4
Tubing connectors	Replace the O-rings	

Table 3-8. User maintenance schedule.

3.2 User maintenance instructions

3.2.1 Cleaning the system

For proper function, the system should be kept dry and clean. Chemical stains and dust should be removed.

1 Wipe the instrument with a soft damp tissue to remove stains.

At the end of the day

If the system will be used with the same buffers the next day, rinse the pump and the system with distilled water as follows:

1 Submerge the appropriate inlet tubing in distilled water.

2 Replace the CFF cassette/cartridge with a T-connector 5/16-24 (code no. 18-1170-59) during cleaning of the system flow path.

3 Run the **System sanitization** method found in the Method Wizard. This method flushes the entire system flow path, including selected inlet and outlet tubings.

Leaving the system for a few days

1 Rinse the entire flow path with distilled water by, for example, using the **System sanitization** method as described in the previous section.

2 Repeat with a bacteriostatic solution, for example, 20% ethanol, having first removed the pH electrode (see instruction below).

The pH electrode should always be stored in a 1:1 mixture of pH 4 buffer and 2 M KNO_3 when not in use. When the pH electrode is removed from the cell holder, the dummy electrode (supplied) must be inserted in the flow path.

CAUTION! Never leave the pH electrode in the cell holder when the system is not used, since this might cause the glass membrane of the electrode to dry out. Remove the pH electrode from the cell holder and fit the end cover filled with a 1:1 mixture of pH 4 buffer and 2 M KNO_3. Do NOT store in water only.

Changing application/process

1 Rinse the entire flow path with distilled water by, for example, using the **System sanitization** method as described above.

2 Run the recommended sanitization procedure. The Method Wizard includes a ready made method for sanitizing the system.

Note: *More information about sanitizing the system is found in the ÄKTAcrossflow User Manual.*

Cleaning methods

The following methods are used before a cross-flow run is performed:

- Rinsing
- Sanitization of the flow path
- CIP of filter (Cleaning-In-Place)
- Water flush of filter
- Water flux test
- Buffer conditioning

All methods listed above are described in detail in *ÄKTAcrossflow User Manual*, *Chapter 5 – Creating Preproduct methods using the Method Wizard*.

3.2.2 Feed pump, transfer pump and permeate pump

Cleaning the inlet and outlet check valves

Faulty operation of the check valves is usually indicated by irregular flow, very low flow or unstable pressure traces. Probable causes are air or dirt in a check valve preventing it from closing to seal and hold the pressure.

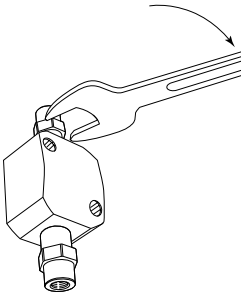
Record the pressure and identify the faulty check valve by observing the pressure trace (see section 4.9). The flow rate should not exceed 10 ml/min.

To clean the check valves in-place on the pump head:

1 Replace the CFF cassette/cartridge with a T-connection 5/16-24 (code no. 18-1170-59).

2 Pump distilled water at 50 ml/min for 2 minutes. This also prevents precipitation of crystals.

3 Pump 100% methanol for approximately 10 minutes.



If this does not correct the problem, follow the instructions below for removing and then cleaning the valves.

Tools required: 16 mm torque wrench

Note: *Flush the check valves with distilled water before removing them.*

Note: *Before removing the check valves, check that all input buffer bottles are placed below the level of the pump heads to prevent siphoning.*

1 Disconnect and remove the tubing.

2 Use the 16 mm wrench to remove the valve from the pump head.

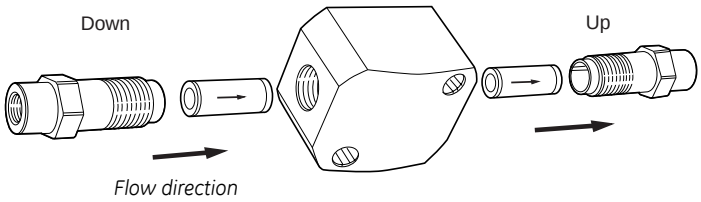
CAUTION! Handle the check valves with care when they have been removed from the pump heads to prevent loss of any internal components.

3 Use a syringe to flush distilled water through the valve to remove salt residues.

4 Immerse the complete valve in methanol and place in an ultrasonic bath for about 5 minutes.

Then repeat the treatment with distilled water.

5 Refit the check valves.



The inlet check valve is fitted to the lower side of the pump head. Tighten the valves using the torque wrench. See Fig 3-14 for the tightening torque values.

CAUTION! Over-tightening might damage threads. Use a torque wrench to tighten the components.

6 Re-fit the tubing.

WARNING! Incorrectly fitted tubing might loosen, causing a jet of liquid to spray out. This is especially dangerous if hazardous chemicals are in use. Connect the tubing by first inserting the tubing fully, then tightening the connector fingertight.

7 Prime the pump carefully and check that the pumping action has been corrected.

CAUTION! Check valves have precision matched components and should not be disassembled further. If the problem cannot be corrected, the check valve should be replaced completely.

3.2.3 Membrane valves

If a membrane does not close or open properly (activating the valve alarm) or if internal leakage appears, the valve might require cleaning.

To clean a membrane valve:

1 Make sure that the valve is filled with 1 M NaOH.

2 Leave it for 15 minutes.

3 Rinse thoroughly with 500 ml de-ionized water.

4 If the valve alarm is still activated, reset the system by switching it off and then on again.

If this does not correct the problem, follow the instructions in section 3.3.3 Membrane valve block to dismount the membrane and clean the valve as follows:

WARNING! The valve is filled with 1 M NaOH. Avoid spillage and wear safety glasses, safety gloves and protective lab coat.

1 Immerse the connection block and the membranes in methanol and place in an ultrasonic bath for about 5 minutes.

2 Repeat the treatment with distilled water.

3 Re-assemble the membrane valve.

If this does not correct the problem, follow the instructions in section 3.3.3 Membrane valve block to replace the membranes.

3.2.4 UV flow cell

Checking UV lamp run time

In the **System Control** module, select **System:Maintenance...** to check the UV lamp run time.

- The lifetime of a Hg lamp at 254 nm in room temperature is typically 7000 hours (in coldroom, typically 2000 h).
- The lifetime of a Hg lamp at 280 nm in room temperature is typically 3500 hours.

When necessary, replace the lamp according to section *Changing the UV lamp*, or contact GE Healthcare for lamp replacement.

Cleaning the UV flow cell off-line

1 Flush a small amount of distilled water through the cell.

2 Connect a 10 ml syringe to the inlet of the cell and squirt distilled water through the cell in small amounts. Then fill the syringe with a 10% surface active detergent solution like *Decon 90*™, *Deconex 11*™, *RBS 25* or equivalent, and squirt five times.

3 After five squirts, leave the detergent solution in the cell for at least 20 minutes.

4 Pump the remaining detergent solution through the cell.

5 Rinse the syringe and flush the cell with distilled water (30 ml).

3.2.5 pH electrode

CAUTION! Never leave the pH electrode in the cell when the system is not used, since this might cause the glass membrane of the electrode to dry out. Remove the pH electrode from the cell and fit the end cover filled with a 1:1 mixture of pH 4 buffer and 2 M KNO_3. Do NOT store in water only.

Cleaning the pH electrode

Note: *The pH electrode has a limited life length and should be replaced every six months or when the response time is slow.*

To improve the response, clean the electrode using one of the following procedures:

- **Salt deposits**: Dissolve the deposit by immersing the electrode first in 0.1 M HCl, then in 0.1 M NaOH, and again in 0.1 M HCl. Each immersion should be for a five-minute period. Rinse the electrode tip in distilled water between each solution.

WARNING! NaOH and HCl are corrosive and therefore dangerous to health. Avoid spillage and wear protective glasses.

- **Oil or grease films**: Wash the electrode tip in a liquid detergent and water. If the film is known to be soluble in a particular organic solvent, wash with this solvent. Rinse the electrode tip in distilled water.

- **Protein deposits**: Dissolve the deposit by immersing the electrode in a solution containing 1% pepsin in 0.1 M HCl. After five minutes, rinse with distilled water.

If these procedures fail to improve the response, try the following procedure:

1 Heat a 1 M KNO_3 solution to 60–80 °C.

2 Place the electrode tip in the heated KNO_3 solution.

3 Allow the electrode to cool while immersed in the KNO_3 solution before re-testing.

If these steps fail to improve the electrode, replace it.

pH electrode regeneration
If the electrode has dried out, immerse its lower end in a 1:1 mixture of pH 4 buffer and 2 M KNO_3 overnight.

3.2.6 Conductivity cell

WARNING! NaOH is corrosive and therefore dangerous to health. Avoid spillage and wear protective glasses.

If the conductivity measurements are not comparable to previous results, the electrodes in the conductivity cell might be contaminated and require cleaning.

To clean the cell:

1 Pump 15 ml of 1 M NaOH at 10 ml/min through the cell by using a syringe.

2 Leave it for 15 minutes.

3 Rinse thoroughly with 500 ml de-ionized water.

Note: *If the cell is totally blocked, the blockage can be broken by carefully using a needle or a piece of string.*

3.2.7 Pressure sensors

WARNING! NaOH is corrosive and therefore dangerous to health. Avoid spillage and wear safety glasses, safety gloves and protective lab coat.

If the pressure measurement seems to be inaccurate, the sensor might require cleaning.

To clean a pressure sensor:

1 Pump 15 ml of 1 M NaOH at 10 ml/min through the pressure sensor either by using a pump or a syringe.

2 Leave it for 15 minutes.

3 Rinse thoroughly with 500 ml de-ionized water.

If this does not correct the problem, dismount the pressure sensor according to the instructions in section 3.3.6 Pressure sensor PP and PR or 3.3.7 Pressure sensor PT (pump outlet manifold) and clean it as follows:

1 Immerse the tubing connection parts in methanol and place in an ultrasonic bath for about 5 minutes.

2 Repeat the treatment with distilled water.

3 Re-assemble the pressure sensor.

3.2.8 Sample inlet air sensor

WARNING! NaOH is corrosive and therefore dangerous to health. Avoid spillage and wear safety glasses, safety gloves and protective lab coat.

If the air sensor does not react when air passes the sensor, it might require cleaning.

To clean an air sensor:

1 Pump 15 ml of 1 M NaOH at 10 ml/min through the air sensor either by using a pump or a syringe.

2 Leave it for 15 minutes.

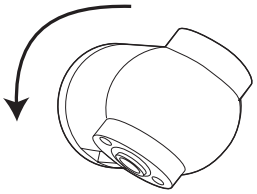
3 Rinse thoroughly with 500 ml de-ionized water.

3.3 Replacing spare parts

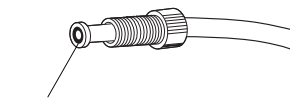
CAUTION! Only use spare parts supplied or specified by GE Healthcare.

3.3.1 General instructions

Some of the components are attached to the instrument unit by a snap connection. These components are detached by turning a quarter of a turn and pulling them off the panel. To attach a component, fit it in the connection and turn it a quarter of a turn until it snaps into position.



Note: *Always make sure that the O-ring does not come loose when disconnecting a 5/16" connector. An O-ring that is stuck in the connector port might cause leakage when re-fitting the connector.*



O-ring

3.3.2 Feed pump P-984 and transfer/permeate pump P-982

If there are signs of liquid leaking between the pump head and the housing side panel, or the volume of the rinsing solution has increased or decreased, replace the piston assembly, liquid chamber and/or glass tube including O-rings of the leaking pump head.

Other typical symptoms of a damaged piston are observed as excessive piston wear, unstable pressure, a reduction in the flow or, in some cases, noise as the piston moves. The piston should be removed, examined for damage or salt precipitation and then replaced with a new piston if necessary.

If a damaged piston has been in operation, the glass tube might be damaged as well and should also be replaced.

If cleaning of a faulty check valve does not improve its performance, it should be replaced.

CAUTION! Do not disassemble the pump head unless there is good reason to believe that there is an internal leakage. Always make sure that sufficient spare components are available before attempting to replace a spare part.

Note: *The power must be switched OFF when removing and refitting the pump heads.*

Note: *Always replace the piston on both pump heads on the P-982 pump, and on all four pump heads on the P-984 pump at the same time.*

Spare parts and tools required:

Seal kit containing (see Ordering information for code no.):
- Piston assembly
- Seal kit (includes O-rings and sealings)
- Check valve, inner
- Check valve, outer
- Glass tube

- 3 mm Allen key
- 16 mm wrench
- 16 mm torque wrench
- Screwdriver, flat-headed, with torque adapter

Note: *Before disassembling the pump heads, move all input buffer bottles below the level of the pump heads to prevent siphoning.*

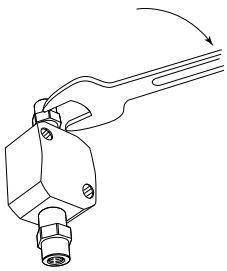
CAUTION! Read the following instructions carefully. Some individual parts of the pump head can be assembled incorrectly. Check the orientation of each part before continuing with the next instruction.

Removing the old piston assembly

1 Switch off the system with the mains power switch on the rear panel of the instrument.

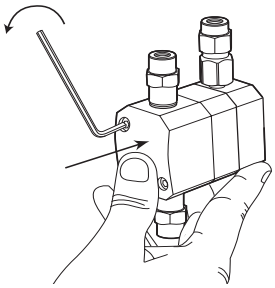
2 Remove the tubing connectors on the inlet and outlet check valves.

3 Remove the rinsing system tubing.



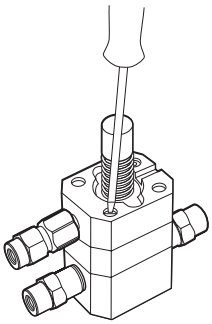
4 If the check valves are also to be checked/replaced, use the wrench to loosen the valves slightly. Do not remove them completely.

5 Using the Allen key, unscrew the two Allen screws locking the pump head in position. Loosen the screws half a turn on each screw at a time while pushing firmly on the front face of the pump head to compensate for the pressure of the piston return spring.



6 Carefully pull out the pump head and place it face down on the bench.

7 Using the flat-headed screwdriver, remove the two screws locking the piston assembly in position. Pull out the piston assembly.



8 Gently pull the glass tube off the piston.

9 Inspect the glass tube using a magnifying glass. Replace with a new glass tube if any scratches or cracks are found.

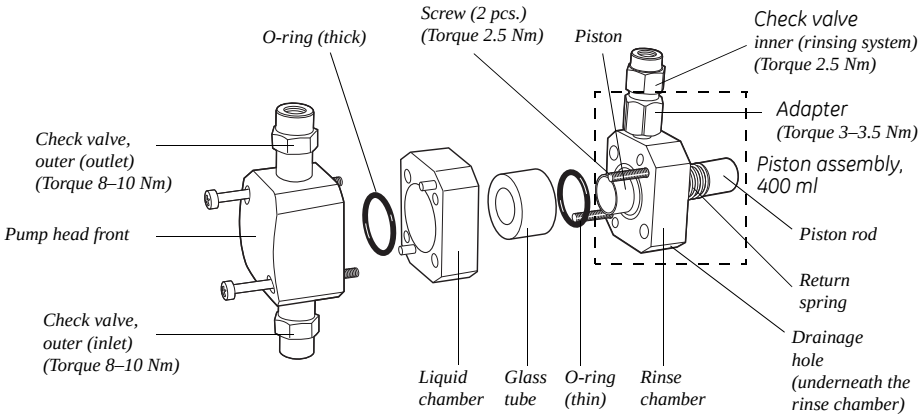


Fig 3-13. Pump head, exploded view.

10 Inspect the piston, piston rod and return spring for signs of damage. If damaged, the piston assembly should be replaced.

11 Wipe the piston with a clean cloth. Inspect the piston with a magnifying glass for scratches. Replace the piston assembly if any scratches or cracks are found.

12 If salt solutions have been used, the piston rod or spring may be slightly corroded. This corrosion can be removed with a rubber eraser. If it cannot be wiped or rubbed clean, scrape off any deposits with a scalpel or razor blade.

Replacing the O-rings

1 Carefully remove and discard the old rinse chamber O-ring.

2 Insert a new O-ring (thin).

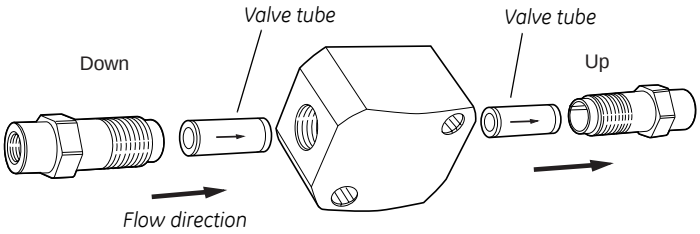
3 Lift off the liquid chamber.

4 Carefully remove and discard the old pump head front O-ring.

5 Insert a new O-ring (thick).

Replacing the outer check valves

1 Unscrew the two loose check valves. Note the direction of the pistons inside the valves. The flow always enters a valve tube through the round hole and exits through the triangular hole.



2 Inspect the nuts and the valve tubes for dirt or damage.

3 Replace with a new check valve if any dirt or damage is found and cleaning does not improve the performance of the old check valve (see section 3.2.2).

Tighten the new check valve using the torque wrench. See Fig 3-14 for the tightening torque value.

CAUTION! Over-tightening might damage threads. Use a torque wrench to tighten the components.

Replacing the inner check valve

1 Use the two wrenches to remove the metal nut of the check valve from the adapter. Note the direction of the valve tube inside the adapter; the round hole faces the rinse chamber.

2 Use a wrench to remove the adapter from the rinse chamber.

3 Inspect the nuts for dirt and damage. Replace the check valve and/or the adapter if required.

Tighten the new check valve and/or adapter using the torque wrench. See Fig 3-14 for the tightening torque values.

CAUTION! Over-tightening might damage threads. Use a torque wrench to tighten the components.

Assembling the new piston head

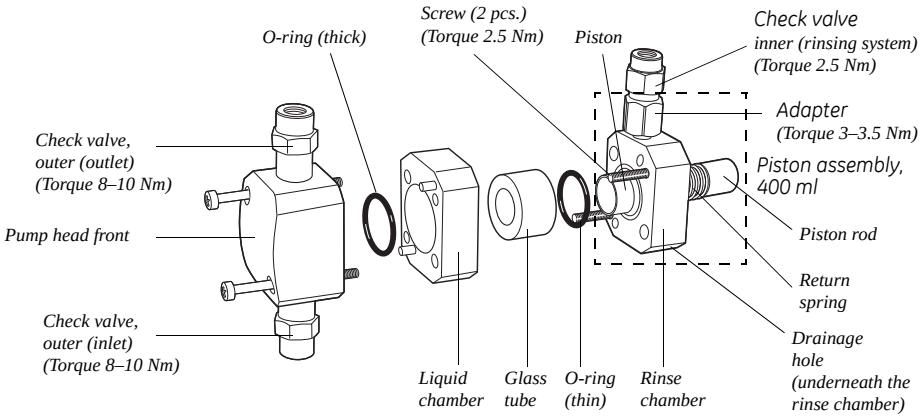


Fig 3-14. Pump head, exploded view.

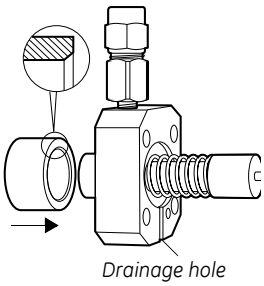
1 Make sure that the new O-rings are installed on the pump head front (thick O-ring) and the rinse chamber (thin O-ring).

2 With the pump head front facing downwards on the bench, place the liquid chamber onto the pump head front.

3 Carefully slide the glass tube onto the piston. Make sure that the tube end that has the largest bevel cutting on the inner edge faces the rinsing system chamber.

4 Insert the glass tube with the piston into the liquid chamber.

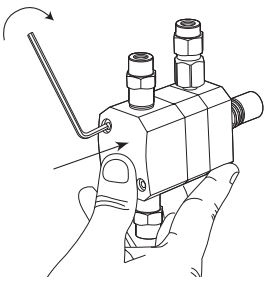
5 Use the two rinse chamber screws to lock the complete pump head together.



Tighten the screws using the screw driver with a torque adapter. See Fig 3-14 for the tightening torque value.

CAUTION! Over-tightening might damage threads. Use a torque wrench to tighten the components.

Installing the pump head



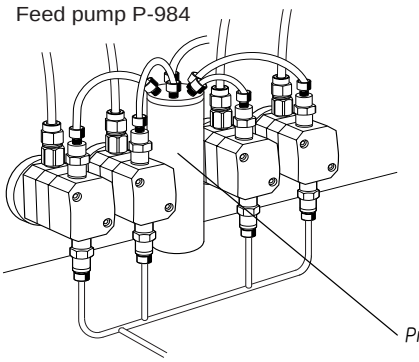
1 Turn the pump head so that **the inner check valve is facing upwards and the drainage hole downwards**. Mount the complete pump head over the locating pins on the front panel.

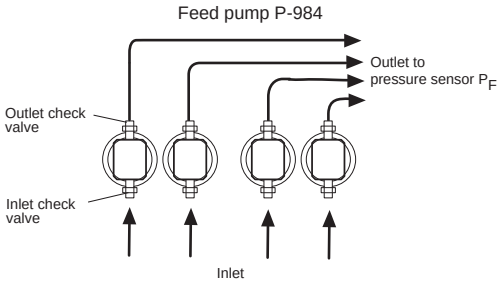
2 Press firmly on the pump head front and use the Allen key to fit and tighten the two retaining screws alternately a little at a time.

Connecting the tubing

WARNING! Incorrectly fitted tubing might loosen, causing a jet of liquid to spray out. This is especially dangerous if hazardous chemicals are in use. Connect the tubing by first inserting the tubing fully, then tightening the connector fingertight.

1 Connect the outlet tubing between the outlet check valve and the sensor P_F. See also section 5.1.7 for the tubing configuration.





2 Connect the rinsing system tubing. See also section 5.1.8 for the tubing configuration.

3 Connect the inlet tubing to the inlet check valve.

4 The pump is ready to be primed. See section 3.4 Priming the system.

3.3.3 Membrane valve block

When replacing the wetted parts of a valve block, the connection block as well as all membranes should be replaced. At normal user maintenance, only the membranes need to be replaced.

Spare parts and tools required:

- Connection block (see Ordering information for code no.)
- Valve membrane (see Ordering information for code no.)

- 7 mm wrench

Removing the connection block and membranes

1 Flush the valve block thoroughly with distilled water.

2 Disconnect all tubing from the valve block.

3 Disconnect the Ethernet cable between the instrument and the computer.

The **Power** indicator on the front panel starts flashing slowly, which indicates that the communication between the computer and the instrument unit is broken. All valves move to closed position.

4 Remove the six attachment screws using the wrench.

5 Carefully loosen the connection block.

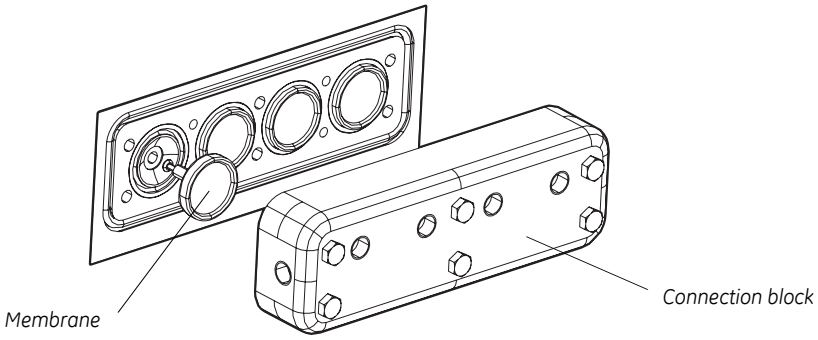


Fig 3-15. Membrane valve block, exploded view.

6 Pull out and discard the old membranes. Be careful not to scratch the mechanical housing of the valve!

Installing the connection block and membranes:

1 Fit the new membranes into position.

2 Carefully fasten the connection block using the attachment screws.

3 Connect the tubing.

4 Connect the Ethernet cable between the instrument and the computer.

5 When the connection between the computer and the instrument unit is established, the valves take up their normal positions in End mode.

3.3.4 Rocker valve block

When replacing the wetted parts of a valve block, the connection block as well as all rockers should be replaced. During normal user maintenance, only the rockers need to be replaced.

Spare parts and tools required:

- Connection block (see Ordering information for code no.)
- Rocker (see Ordering information for code no.)

- 7 mm wrench

Removing the connection block and rockers

1 Flush the valve block thoroughly with distilled water.

2 Disconnect all tubing from the valve block.

3 Disconnect the Ethernet cable between the instrument and the computer.

The **Power** indicator on the front panel starts flashing slowly, which indicates that the communication between the computer and the instrument unit is broken. All valves move to closed position.

4 Remove the six attachment screws using the wrench.

5 Carefully loosen the connection block.

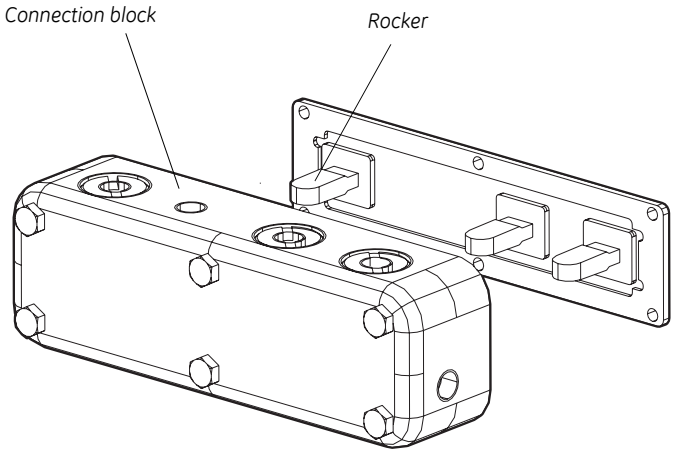
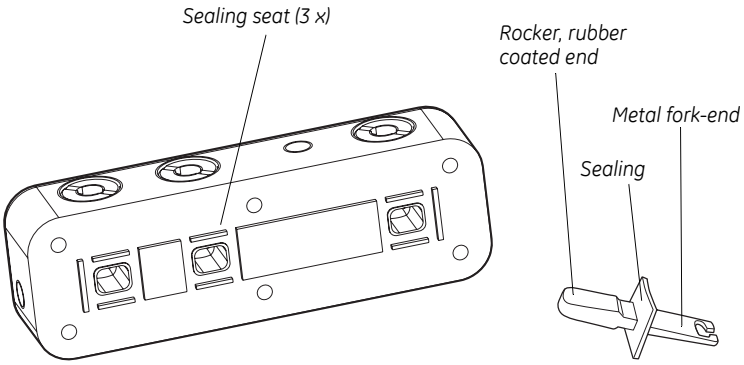


Fig 3-16. Rocker valve block, exploded view.

6 Pull out and discard the old rockers. Be careful not to scratch the mechanical housing of the valve!

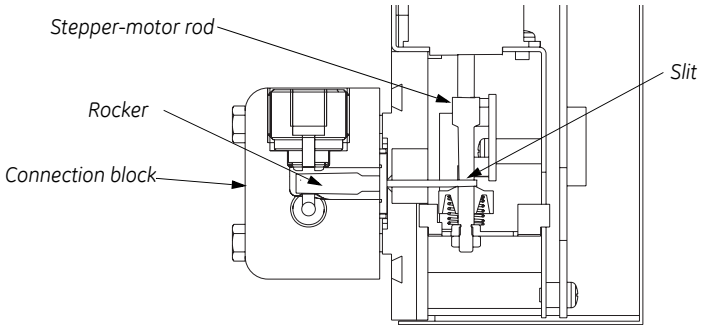
Installing the connection block and rockers

1 Insert the rubber coated end of the new rockers into the connection block. Check that the rectangular sealing fits correctly to its counterpart.



2 Insert the fork-shaped metal end of the rocker into the slit on the instrument front panel. Check that the metal fork-end is mated to the slit in

the stepper-motor rod inside the front panel of the instrument, see figure below.



3 Attach the connection block to the front panel by tightening the six attachment screws.

4 Re-connect the tubing.

5 Connect the Ethernet cable between the instrument and the computer.

6 When the connection between the computer and the instrument unit is established, the valves take up their normal positions in End mode.

3.3.5 2-way transfer purge valve and pressure modulating/control valves R-PCV and P-PCV

Spare parts and tools required:

- Rocker (see Ordering information for code no.)

- 3 mm Allen key

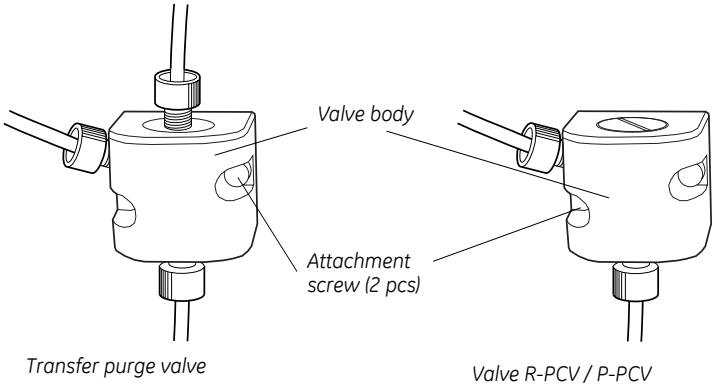
Remove the rocker

1 Flush the valve thoroughly with distilled water.

2 Switch off the system with the mains power switch.

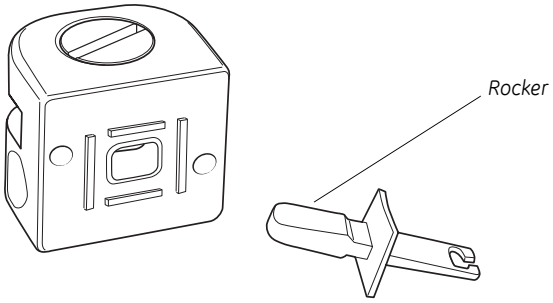
3 Disconnect the tubing from the valve.

4 Loosen the two attachment screws using the Allen key.



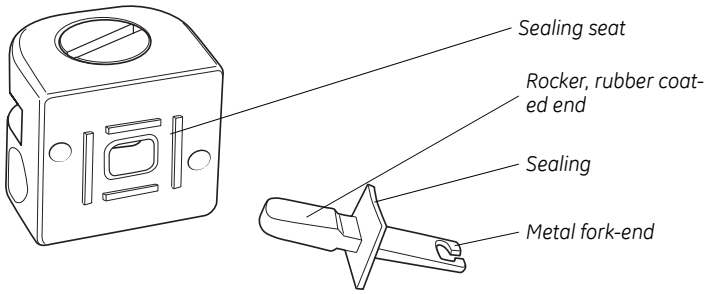
5 Remove the valve body by pulling it outwards from the front panel.

6 Pull out and discard the old rocker from the valve body, see figure below.

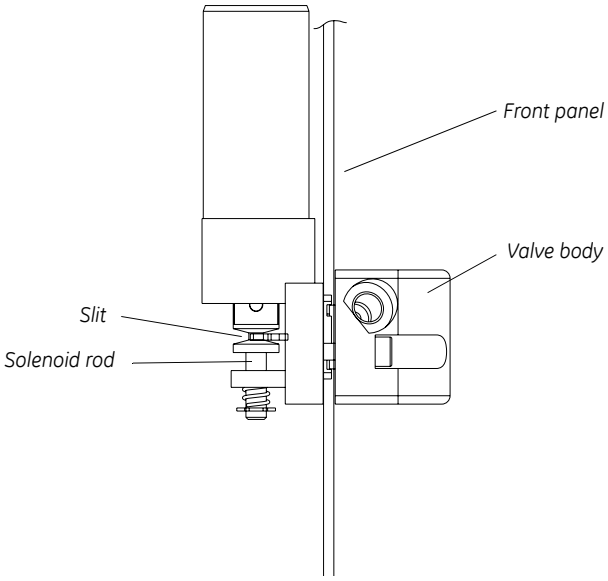


Installing the new rocker

1 Insert the rubber coated end of the new rocker into the valve body. Check that the rectangular sealing fits correctly to its counterpart.



2 Insert the fork-shaped metal end of the rocker into the slit on the instrument front panel. Check that the metal fork-end is mated to the slit in the solenoid rod inside the front panel of the instrument, see figure below.



3 Attach the valve body to the front panel by tightening the two attachment screws.

4 Re-connect the tubing.

3.3.6 Pressure sensor P_P and P_R

Spare parts and tools required:

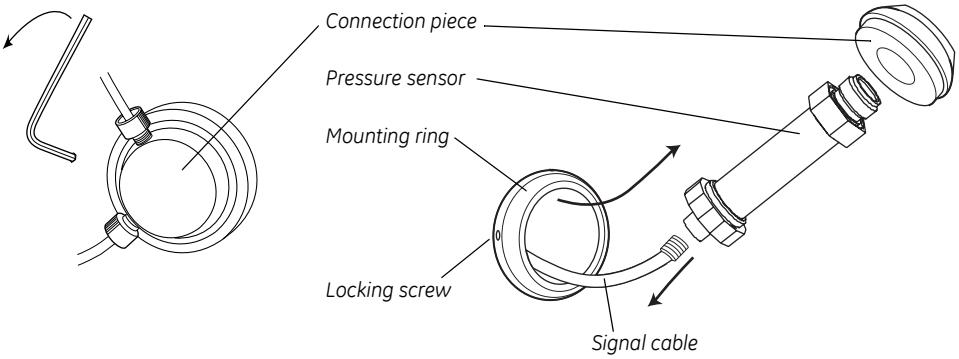
- Pressure sensor (see Ordering information for code no.)

- 1.5 mm Allen key

1 Flush the pressure sensor thoroughly with distilled water.

2 Switch off the system with the mains power switch.

3 Disconnect the tubing from the connection piece.



4 Loosen the locking screw at the left-hand side of the mounting ring using the Allen key.

5 Carefully pull out the connection piece with the pressure sensor from the mounting ring.

6 Disconnect the signal cable from the pressure sensor.

7 Unscrew and remove the pressure sensor from the connection piece.

Tip! Use stop plugs in the inlet and outlet ports as holders when unscrewing the pressure sensor from the connection piece.

8 Mount the new pressure sensor to the connection piece.

9 Connect the signal cable to the new pressure sensor and insert it into the mounting ring.

10 Tighten the locking screw.

11 Check the O-rings at the tubing ends and connect the tubing.

3.3.7 Pressure sensor P_T (pump outlet manifold)

Spare parts and tools required:

- Pressure sensor P_T incl. outlet manifold (see Ordering information for code no.)

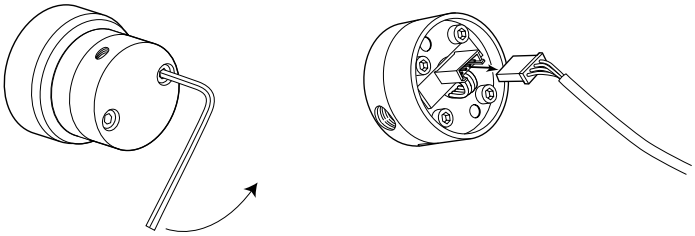
- 3 mm Allen key

1 Flush the outlet pressure sensor thoroughly with distilled water.

2 Switch off the system with the mains power switch.

3 Disconnect all tubing from the pressure sensor.

4 Loosen the two attachment screws using the Allen key.



5 Gently pull out the outlet manifold.

6 Disconnect the signal cable.

7 Connect the cable to the new pressure sensor.

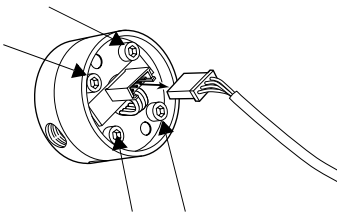
8 Fit the sensor into position.

9 Carefully fasten the sensor using the attachment screws. Tighten the screws alternately a little at a time.

10 Connect the tubing.

11 Calibrate the new pressure sensor according to section 2.3.1.

To allow cleaning of the flow path inside the pressure sensor, loosen the four attachment screws at the rear of the sensor and remove the rear part.



3.3.8 Pressure sensor P_F

Spare parts and tools required:

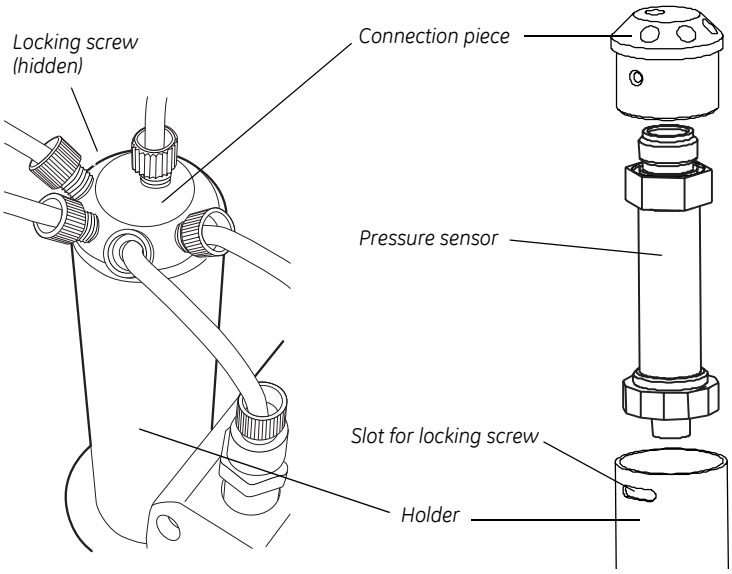
- Pressure sensor (see Ordering information for code no.)

- Phillips screwdriver

1 Flush the pressure sensor thoroughly with distilled water.

2 Switch off the system with the mains power switch.

3 Disconnect the tubing from the connection piece.



4 Loosen the locking screw.

5 Pull out the pressure sensor with the connection piece from the holder.

6 Unscrew and remove the pressure sensor from the connection piece.

7 Disconnect the signal cable from the pressure sensor.

8 Mount the new pressure sensor to the connection piece and connect the signal cable, then insert into the holder.

9 Tighten the locking screw.

10 Check the O-rings at the tubing ends and connect the tubing.

3.3.9 Air sensor

Spare part required:

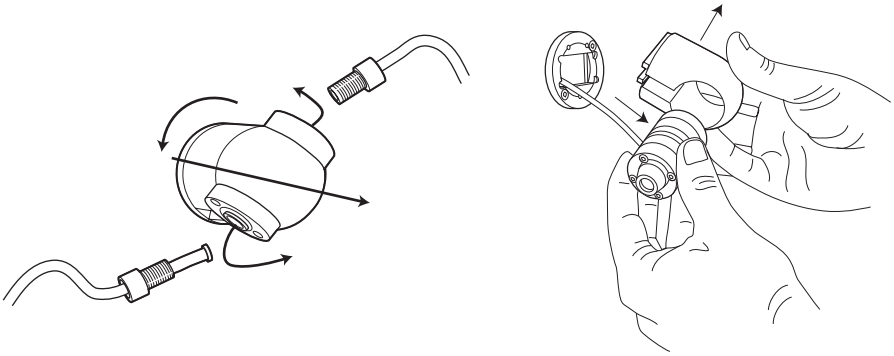
- Sample inlet air sensor (see Ordering information for code no.)

Sample inlet air sensor

1 Flush the air sensor thoroughly with distilled water and stop the pump.

2 Switch off the system with the mains power switch.

3 Disconnect the tubing from the air sensor.

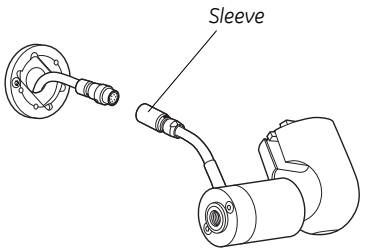


4 Release the air sensor holder from the panel by turning the holder a quarter of a turn.

5 Loosen the stop screw to the signal cable.

6 Gently pull out the signal cable to reach the connector.

7 Disconnect the push-pull connector by pulling the sleeve and remove the air sensor.



8 Connect the cable from the new air sensor to the connector.

9 Tighten the signal cable stop screw.

10 Fit the new air sensor in the holder.

11 Fasten the holder on the panel.

12 Connect the tubing.

3.3.10 UV flow cell

Spare parts and tools required:

- UV flow cell (see Ordering information for code no.)

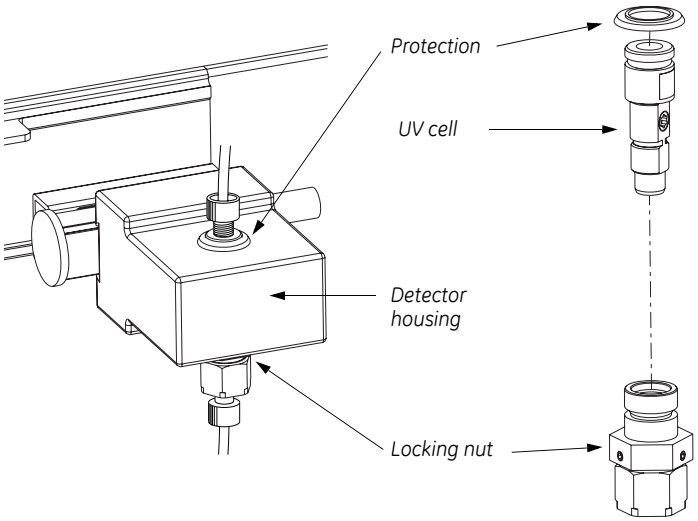
- Screwdriver, small flat-headed
- 22 mm wrench

Removing the UV flow cell

1 Flush the cell with distilled water.

2 Switch off mains power to the system.

3 Disconnect the tubing from the UV cell.

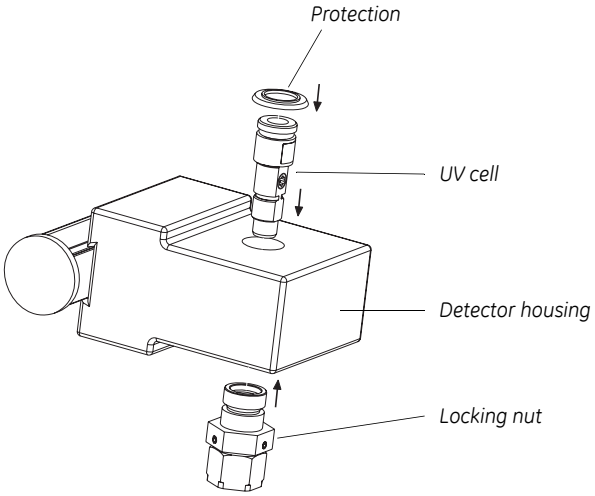


4 Remove the UV cell from the detector housing as follows:

- Loosen and remove the protection.
- Loosen and remove the locking nut.
- Remove the UV cell

UV flow cell installation

1 Insert the UV cell into the detector housing from above.



Note: *The UV cell can only be placed in one correct position.*

2 Secure the UV cell by turning the locking nut until it reaches the stop position. Tighten firmly.

Note: *If the locking nut is not tightened sufficiently, the monitor will function poorly (e.g. drifting base-line).*

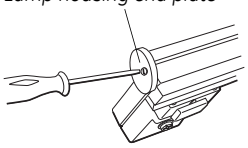
3 Attach the protection by pushing it downwards.

Note: *Avoid spillage for prolonged monitor lifetime.*

Changing lamp assembly

WARNING! The module uses high intensity ultra-violet light. Do not remove the UV lamp while the instrument is running. Before changing a UV lamp, ensure that the mains power is turned off to prevent injury to eyes. If the mercury lamp is broken, make sure that all mercury is removed and disposed of according to national and local environmental regulations.

Lamp housing end plate



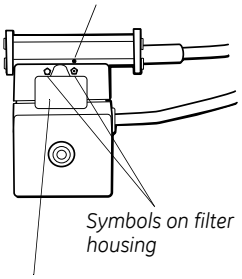
1 Use a Phillips screwdriver to detach the end plate by removing one and loosening the other of the two holding screws on the lamp housing to be removed.

2 Slide the lamp housing off the filter housing.

3 Detach the end plate, as in step 1 above, from the lamp housing to be fitted to the optical unit.

4 Slide the lamp housing onto the filter housing. The lamp and signal cables should be on the same side. As you slide the lamp housing into position, depress the two pressure pads on the filter housing in sequence to facilitate the installation.

Dot on lamp housing



5 Refit the lamp housing end plate.

6 Slide the lamp housing firmly into place. There will be a faint click when the housing is positioned correctly. The Hg lamp housing can take up two positions, one for 280 nm, marked by ◻ on the filter housing, and the other marked by ● for all other wavelengths. The Zn lamp housing has only one position.

7 Set the wavelength to be used by selecting lamp position (indicated by a dot on the lamp housing) in combination with the appropriate filter, i.e. the dot on the lamp housing should be adjacent to the symbol on the filter housing corresponding to the symbol on the filter wheel for the filter to be used. A click will indicate that the filter is in position.

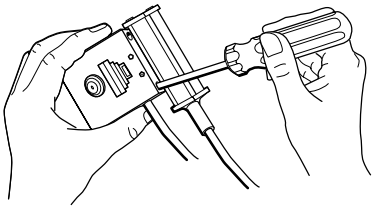
Note: *In UNICORN, the wavelength used set in the method notes.*

Filter change

The Hg optics with 254 and 280 nm filters and the Zn optics with the 214 nm filter are delivered with filters installed. If other filters are to be used, install the new filters as described in section Installing optical filters (optional).

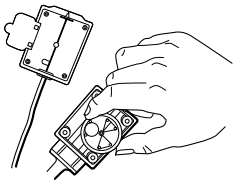
Installing optical filters (optional)

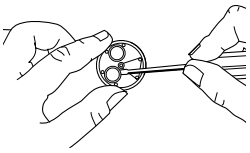
The Hg optics with 254 and 280 nm filters and the Zn optics with the 214 nm filter are delivered with filters installed. If other filters are to be used, install them as follows:



1 If the Zn lamp is attached, remove the lamp housing as described in section *Changing the UV lamp*.

2 Remove the four screws in the filter housing. Separate the filter housing from the detector housing.



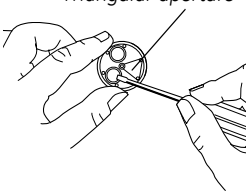


3 Carefully remove the filter wheel from the filter housing.

4 If necessary, remove the filter(s) from the filter wheel by pressing it (them) out, e.g. with a small screwdriver.

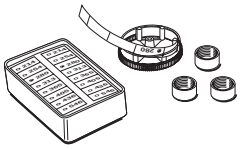
Note: *Filters are sensitive optical components. Never touch the optical surfaces or expose them to temperatures above 60 °C. Clean them with dry lens cleaning tissue and store them, when not in use, in the box in which they were supplied. Heavy contamination may be removed by using a lens tissue dipped in ethanol.*

Triangular aperture



5 Insert the filter(s) of choice into the filter wheel (maximum 3 filters) with the correct orientation (the mirror side facing upwards) and position over one of the three triangular apertures. The filters snap in by pressing them quite firmly. Do not touch the filter surface.

6 Remove the circular plastic band showing the wavelength(s).



7 Remove labels from the band if necessary.

8 Place the correct labels on the band with the label designation facing outwards. Ensure that the label position corresponds to the filter position, i.e. the label should be placed opposite the filter.

9 Reassemble the circular plastic band with the filter wheel peg fitting into the band notch.

10 Check that all filters are clean. Insert the filter wheel back into the filter housing.

Note: *The filter wheel can only be placed in the correct position.*

11 Reassemble the filter housing with the detector housing by fastening the four screws.

Changing the UV lamp

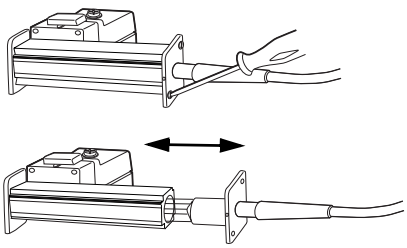
WARNING! The module uses high intensity ultra-violet light. Do not remove the UV lamp while the instrument is running. Before changing a UV lamp, ensure that the mains power is turned off to prevent injury to eyes. If the mercury lamp is broken, make sure that all mercury is removed and disposed of according to national and local environmental regulations.

1 Remove the two screws on the lamp housing end plate that is attached to the power cable.

2 Carefully slide the lamp out of the lamp housing.

3 Without touching the lamp glass, insert the new lamp into the lamp housing and secure the end plate with the two screws.

Unscrewing the lamp



Removing/inserting the lamp

3.3.11 pH electrode

Spare parts and tools required:

- pH electrode, ÄKTAcrossflow

- Cell holder, pH (see Ordering information for code nos.)
- Phillips screwdriver

Replacing the pH electrode

CAUTION! Handle the pH electrode with care. The tip of the pH electrode consists of a thin glass membrane. Protect it from breakage, contamination and drying out or the electrode will be destroyed. Always store the pH electrode with the end cover filled with a 1:1 mixture of pH 4 buffer and 2 M KNO_3. Do NOT store in water only.

1 Switch off the system with the mains power switch.

2 Unscrew the cable connector at the top of the old pH electrode.

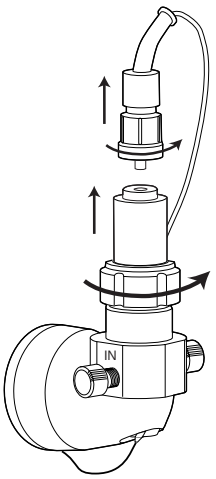
3 Unscrew the locking nut that secures the pH electrode.

4 Remove the pH electrode.

5 Unpack the new pH electrode.

6 Remove the end cover. Make sure that it is not broken or dry.

7 Before using the electrode, immerse the glass tip in a pH 4 buffer solution for 30 minutes.



8 Carefully insert the electrode in the cell holder. Tighten the locking nut by hand to secure the electrode.

9 Fit the signal cable to the top of the pH electrode.

Replacing the cell holder

1 Flush the cell holder with distilled water.

2 Disconnect the tubing.

3 Disconnect the signal cable from the top of the pH electrode (if used).

4 Move the pH electrode or the dummy electrode to the new cell holder.

5 Remove the ground wire from the cell holder using the Phillips screwdriver.

6 Release the old cell holder from the panel by turning it a quarter of a turn.

7 Fasten the new cell holder on the panel.

8 Connect the tubing.

9 Connect the signal cable to the pH electrode (if used).

3.3.12 Conductivity cell

Spare parts required:

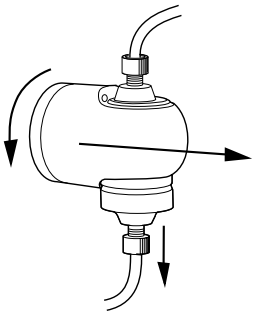
- Conductivity cell (see Ordering information for code no.)

1 Flush the cell with distilled water.

2 Switch off the system with the mains power switch.

3 Disconnect the tubing.

4 Release the conductivity cell holder from the panel by turning it a quarter of a turn. Gently push down the cell if necessary.



5 Loosen the stop screw to the signal cable.

6 Gently remove the old conductivity cell from the holder and disconnect the push-pull cable connector.

7 Connect the cable to the new conductivity cell and put the cell in the holder. Make sure that the screw head end on the conductivity cell faces downwards!

8 Tighten the signal cable stop screw.

9 Connect the tubing.

3.4 Priming the system

3.4.1 Manual priming

To prime the transfer pump and inlet tubing manually:

1 Fill a flask with distilled water and immerse the appropriate valve block (**T-VB-In**) inlet tubing in the water.

2 Connect a 5/16" connector to the waste tubing.

3 Connect a 5/16" female/M6 male union to the tubing.

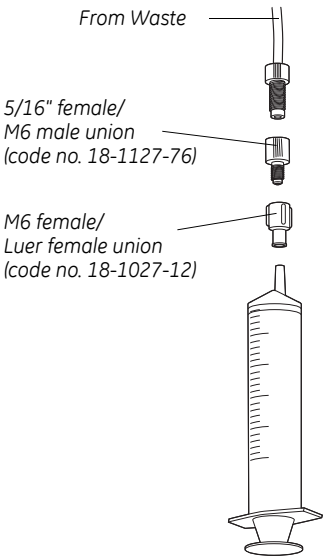
4 Connect a M6 female/Luer female union to the first union.

5 Fit an empty male Luer syringe (> 25 ml) to the Luer union.

6 In the **System Control** module, select **Manual:Transfer:TransferValveblocks ,** and then select **TransferPurgeValve Waste**.

7 Open the appropriate inlet valve and **Waste**.

8 Use the syringe to draw water through the inlet tubing and pump until it starts to enter the syringe.



3.5 Preventive maintenance

GE Healthcare recommends that preventive maintenance (PM) is performed by qualified service personnel during the yearly service visit. The scope of PM is to be agreed in the service contract.

4 Troubleshooting

This chapter provides troubleshooting guidelines. The troubleshooting guide focuses on error symptoms related to monitor curves and operation of the individual components.

Monitor curve/Component	Page
Feed pump, transfer pump and permeate pump	88
Membrane valves	89
Pressure sensors	89
Pressure curve	90
Conductivity curve	90
UV curve	91
Air sensor	92

If the suggested actions do not correct the fault, call GE Healthcare Service.

4.1 Feed pump, transfer pump and permeate pump

Error symptom	Possible cause	Corrective action
Liquid leaking between the pump head and the instrument panel	Piston, glass tube, liquid chamber or O-rings incorrectly fitted or worn	Replace the piston assembly, glass tube, and/or O-rings in the pump head. See section 3.3.2.
Low buffer flow and noise	Bad piston spring	Disassemble the pump head and examine the piston spring. Replace the piston assembly if necessary.
		If the spring is corroded, check piston, glass tube, and/or O-rings. Make sure that the rinsing system is always used when working with aqueous buffers with high salt concentration.
		If the piston is damaged, replace it according to section 3.3.2 Replace the piston assembly, glass tube, and/or O-rings with new components
Leakage around a tubing connector	Leaking connection and/or crystallized material around the tubing connector	Unscrew the connector and check if it is worn or incorrectly fitted. If required, replace the connector. Tighten the connector with your fingers only.
Erratic pump pressure	Air trapped in the pump heads	Check the pump function by observing the pressure curve in UNICORN. By observing the pressure trace, the pump head which is functioning abnormally can be identified. Some examples of normal and abnormal pressure traces, together with comments, are shown in section 4.9.
	Leaking connectors	
	Piston leakage	
	Piston damaged	
	Check valve malfunction	

4.2 Membrane valves

Error symptoms	Possible causes	Action
External leakage	Leaking tubing connectors	Check the tubing connectors. Tighten or replace if necessary.
Internal leakage (can be detected underneath the valve body)	The valve membrane might be worn or damaged	Change the valve membrane. See section 3.3.3.
High back-pressure	Dirt in the flow path	Clean the valve according to section 3.2.3
		Change the valve membrane. See section 3.3.3.
Valve alarm	A valve membrane might be damaged	Change the valve membrane. See section 3.3.3.

4.3 Pressure sensors

Error symptoms	Possible causes	Action
External leakage	Leaking tubing connectors	Check the tubing connectors. Tighten or replace if necessary.
High back-pressure	Dirt in the flow path	Clean the pressure sensor according to section 3.2.7
		Change the pressure sensor. See section 3.3.

4.4 Pressure curve

Error symptom	Possible cause	Corrective action
Erratic flow, noisy baseline signal, irregular pressure trace Note: Make sure that no control mode is active!	Air bubbles passing through or trapped in the pump	Check that there is sufficient buffer in the reservoirs
		Check all connections for leaks
	Inlet or outlet check valves not functioning correctly	Remove any dirt in the valves by cleaning according to section 3.2.2
	Piston assembly leaking	Replace the piston assembly, glass tube, and/or O-rings in the pump head. See section 3.3.2.
	Blockage or partial blockage of flow path	Flush through to clear blockage
		If necessary, replace tubing

4.5 Conductivity curve

Error symptom	Possible cause	Corrective action
Baseline drift or noisy signal	Leaking tubing connections	Tighten the connectors. If necessary, replace the connectors.
	Bad pump	See sections 3.3.2
	Dirty conductivity cell	Clean the conductivity cell according to section 3.2.6
	No flow through UV cell	Check for appropriate control mode.
Conductivity measurement with the same buffer appears to decrease over time	Dirty conductivity cell	Clean the conductivity cell according to section 3.2.6
	The ambient temperature may have decreased	Use a temperature compensation factor, see section 2.3.3
Absolute conductivity value is wrong	Bad calibration	Calibrate the conductivity cell, see section 2.3.3
	Calibration solution, 1.00 M NaCl, not correctly prepared	Recalibrate using a new calibration solution

Error symptom	Possible cause	Corrective action
Incorrect or unstable reading	Bad pump or membrane valve function	Check the pump and the valves
	The temperature compensation not properly set	Check that the temperature sensor Temp is calibrated, and that the correct temperature compensation factor is in use. See section 2.3.3.
	The CFF cassette/cartridge not equilibrated	Equilibrate the cassette/cartridge. If necessary, clean the cassette/cartridge.

4.6 UV curve

Error symptom	Possible cause	Corrective action
Ghost peaks	Dirt or residues in the flow path from previous runs	Clean the system according to section 3.2.1
	Residues in the CFF cassette/ cartridge from previous runs	Clean the CFF cassette/cartridge according to instructions
Noisy UV-signal, signal drift or instability	Bad cable connections	Check that the UV cell is properly attached to the panel
	No flow through UV cell	Check for appropriate control mode.
	Dirty UV cell	Clean the UV cell, refer to section 3.2.4
	Damaged membrane	Check if the signal is still noisy with water.

4.7 Air sensor

Error symptoms	Possible causes	Action
External leakage	Leaking tubing connectors	Check the tubing connectors. Tighten or replace if necessary.
High back-pressure	Dirt in the flow path	Clean the air sensor according to section 3.2.8
		Change the air sensor. See section 3.3.9.

4.8 Installation Test.

Failed Unit	Possible cause	Corrective action
T-VB-in 1 to 8	Mismatch between in and out volumes.	
	Air is drawn in.	Check all fingertights.
	Inlet tubing is not immersed in the water.	Make sure that the inlet tube is immersed in water.
	Reservoir was not empty from the start.	Repeat the test with the reservoir empty from the beginning.
	Obstruction in the flow path.	Check all flow paths and replace if necessary.
	Transfer valve blocked.	Disassemble the connection block and clean it.
	The transfer purge valve is leaking.	Contact your GEHC Service representative for replacement of the valve.
	The level sensor is broken.	Replace the level sensor. Make sure the system is in End mode before starting the system.
R-VB-Out 1 to 3	The retentate valve outlet does not provide enough counter pressure.	
	Old valve block is used.	No action is required since the old valve block will not provide any back pressure.

Failed Unit	Possible cause	Corrective action
	Retentate valve incorrectly calibrated.	The retentate valve is incorrectly calibrated. Contact your GEHC Service representative.
Cond sensor	The Cond value did reach its limit	Check calibration/ Check test solution
UV sensor	The UV did not reach its limit. Wrong UV filter installed.	Check filter settings / Check test solution Make sure the 280 mm filter is installed and the position of the lamp housing is correct.
pH sensor	The pH value did not reach its limit. Sensor not calibrated Sensor broken.	Check calibration/ Check test solution Calibrate the sensor Replace the sensor.
R-PCV / P-PCV	The R-PCV or the P-PCV valve did not provide enough counter pressure.	Contact your GEHC Service representative.
Pressure sensors	The sensor did not detect any pressure Pressure sensor broken R-PCV or P-PCV broken	Check for leakage Contact your GEHC Service representative for replacement of broken parts Contact your GEHC Service representative for replacement of broken parts
Pump flow detection	The pump did not report any flow.	Contact your GEHC Service representative.
Air sensor	Air sensor broken.	Contact your GEHC Service representative.
Permeate outlets	High pressure alarm.	Disassemble and clean the permeate valve outlets. If this does not work, call service.

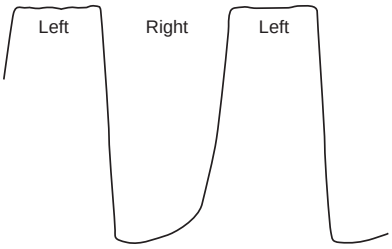
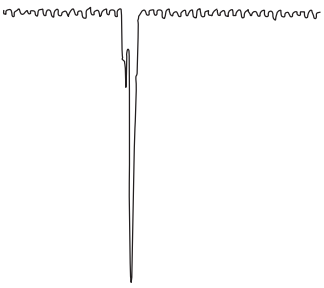
4.9 Checking the pump pressure

To check the pump function, check the pressure curve in UNICORN.

There can be several causes of an abnormal pressure recording, for example:

- Air trapped in the pump heads.
- Leaking connections.
- Piston seal leakage.
- Check valve malfunction.
- Piston damaged.

Some examples of abnormal pressure traces, together with comments, are shown in Table 4-9 .

Result	***Diagnosis***
	Left pump head OK, right pump head not working. Possible causes: • Bad piston. • Major leakage in inlet check valve. • Inlet blocked. • Glass tube broken.
	Air bubbles passing through pump heads

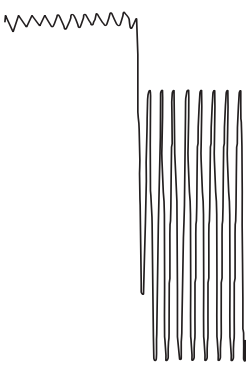
Result	*Diagnosis*
	One pump head has stopped working. Possible causes: • Major leakage in one pump head. • Major leakage in inlet check valve. • Inlet blocked. • Bad pump calibration.

Table 4-9. Abnormal pressure traces.

5 Reference information

5.1 System description

5.1.1 ÄKTAcrossflow system

ÄKTAcrossflow is a high performance, automated filtration system. ÄKTAcrossflow consists of an instrument unit and a Windows-based computer running UNICORN version 5.10 or higher.

The purpose of the ÄKTAcrossflow system is to facilitate process development and optimization of ultrafiltation/diafiltration (UF/DF) and microfiltration (MF) operations.

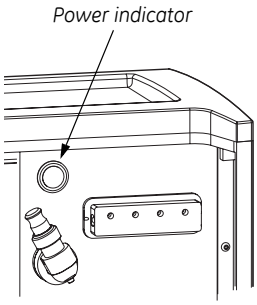
The system is designed and optimized for operation in conjunction with the following membrane cassettes/cartridges:

- Flat sheet membrane (50 cm^2 and 100 cm^2) in UF/DF applications.
- Hollow fiber membrane (40 cm^2 and 50 cm^2) in UF/DF and MF applications.

Fig 5-17. The ÄKTAcrossflow instrument unit.

5.1.2 Indicator and switch on the instrument unit

The ÄKTAcrossflow instrument is equipped with the following indicator and mains switch.



Indicator/Switch	Color	Description
Power (indicator)	Green	1. Flashes slowly until the internal communication with the CU (Control Unit) is established 2. Steady light when the internal communication with the CU is established. 3. Steady light when UNICORN is connected to the instrument unit.
Power (mains switch)	–	Switches on/off power to the instrument. Located on the rear panel.

Table 5-10. Indicator and mains switch on the instrument unit.

5.1.3 Component location

The location of each of the main components of ÄKTAcrossflow instrument unit is shown in Fig 5-18 and Fig 5-20.

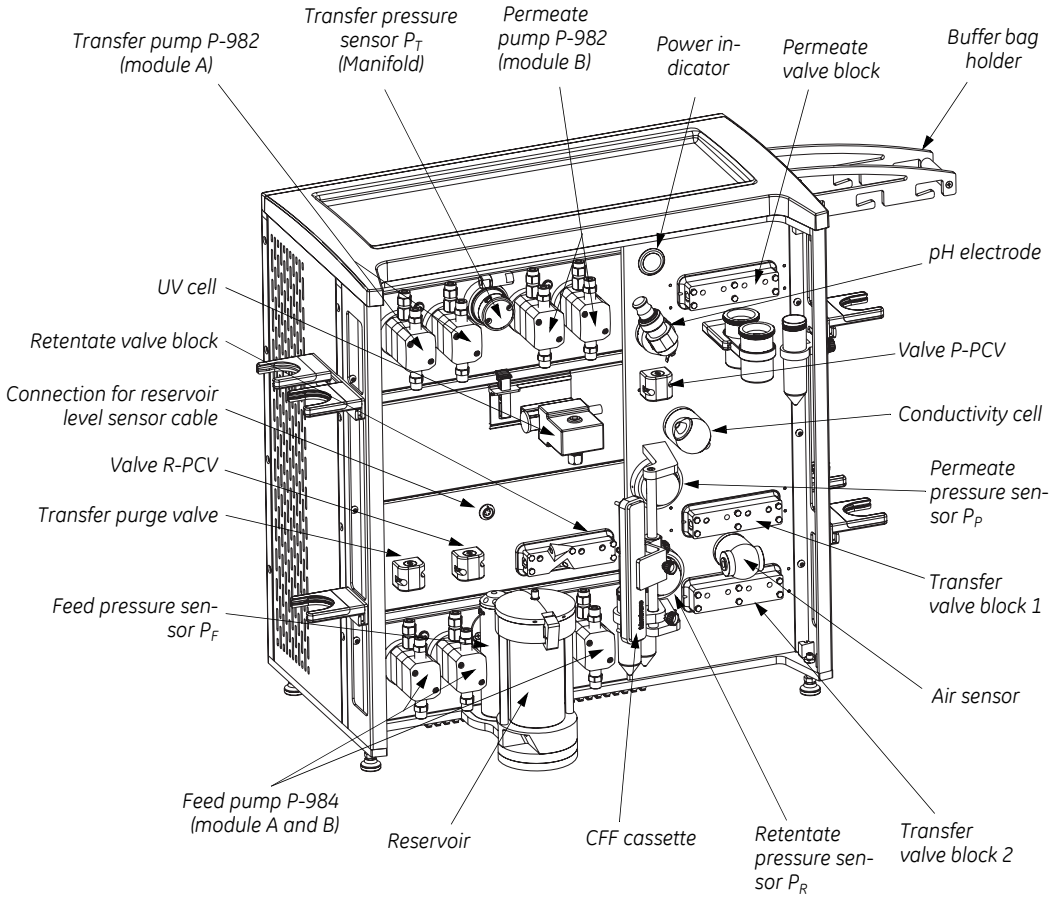


Fig 5-18. Location of ÄKTAcrossflow components.

Buffer bag holder

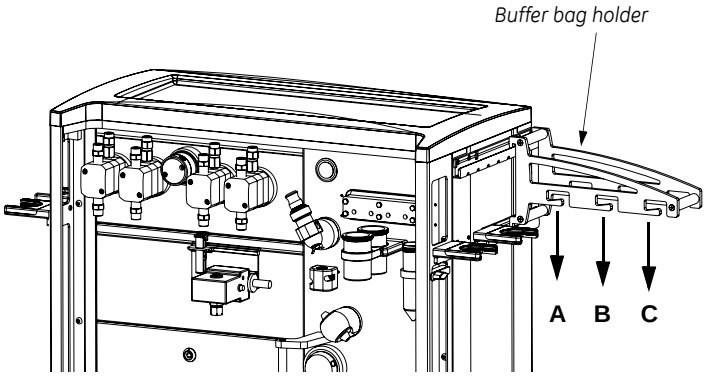


Fig 5-19. Buffer bag holder.

The bag holder can be placed in two positions, in the rear position as shown in the figure above, and in the fore position.

Maximum allowed weight on the bag holder:

- Pos. A + pos. B + pos. C = 15 kg.

Bottles

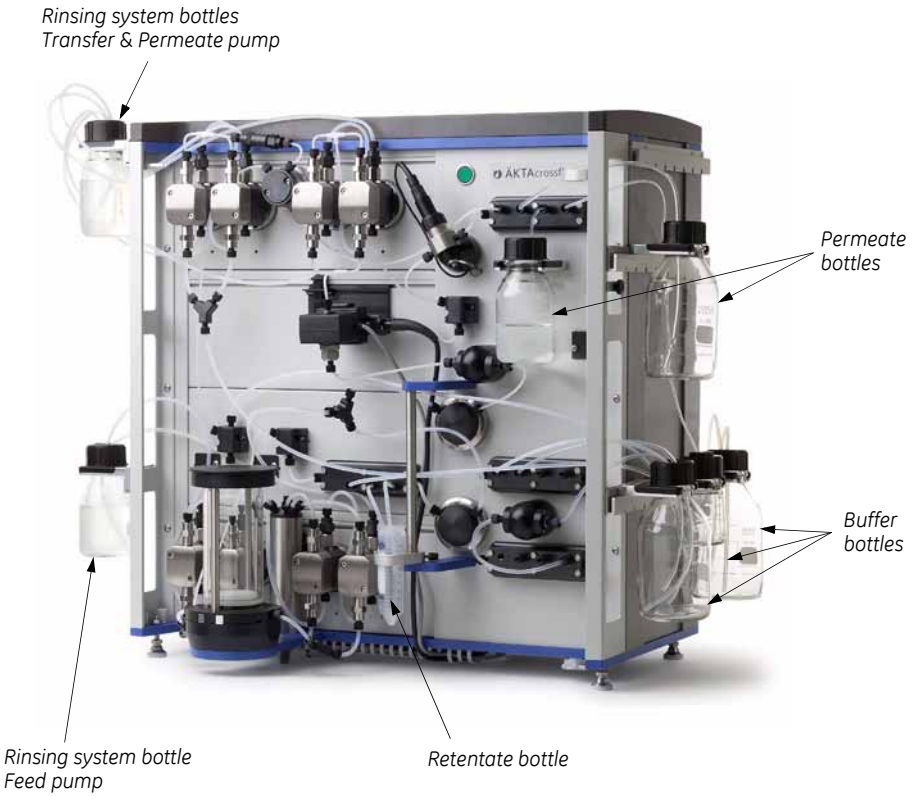


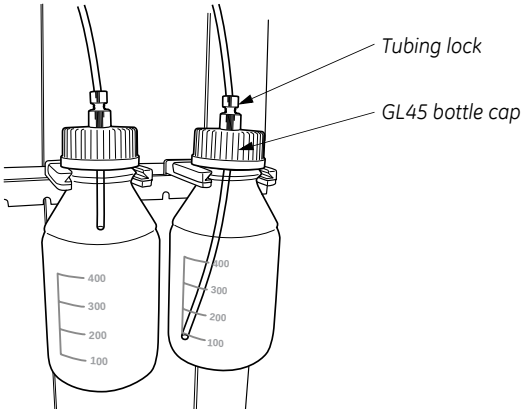
Fig 5-20. Location of bottles.

Bottle	Volume [ml]	Qty	Comment
Buffer	500	3	Schott GL45
Retentate & permeate	50	1+1	Falcon
Permeate	250	2	Schott GL45
Rinsing system, transfer & permeate pump	500	2	Schott GL45
Rinsing system, feed pump	500	1	Schott GL45

Table 5-11. Bottles recommended for ÄKTAcrossflow.

Tubing lock

To prevent siphoning in the waste tubing, the GL45 bottle cap has a tubing lock to make it easy to lock the tubing end at a high position inside the bottle, see figure below:



When using the tubing lock on the inlet side bottles, the bottle can be emptied completely by locking the tubing end at the lowest position.

5.1.4 Electrical connections

Mains cable

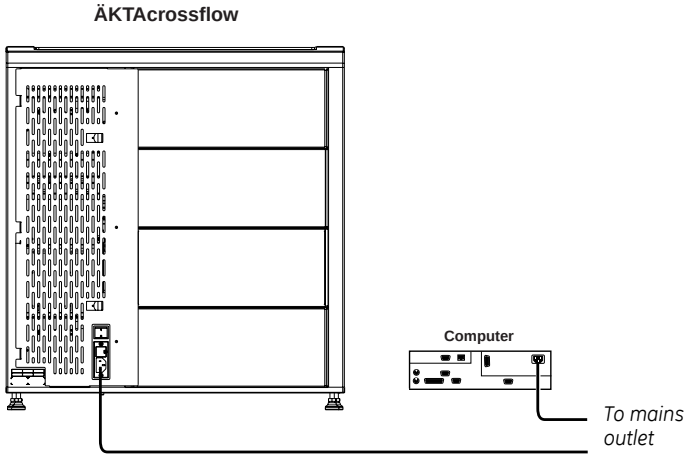


Fig 5-21. Mains cables.

One end of the supplied mains cable is connected to the ÄKTAcrossflow mains inlet, and the other end to a mains supply outlet with protective ground.

One end of the supplied mains cable is connected to the PC mains inlet, and the other end to a mains supply outlet with protective ground.

CAUTION! The free mains outlet inside the ÄKTAcrossflow instrument is intended for connection of the fraction collector Frac-920 only.

5.1.5 Mains fuse

The mains input fuse is located at the mains power inlet on the rear panel of the ÄKTAcrossflow.

WARNING! Always disconnect the mains supply before removing the mains fuse. For continued protection against risk of fire, replace only with fuse of the same type and rating.

Replacing the mains fuse

1 Turn off the power to ÄKTAcrossflow.

2 Disconnect the mains cable from the mains power inlet.

3 Locate the fuse drawer on the connector panel.

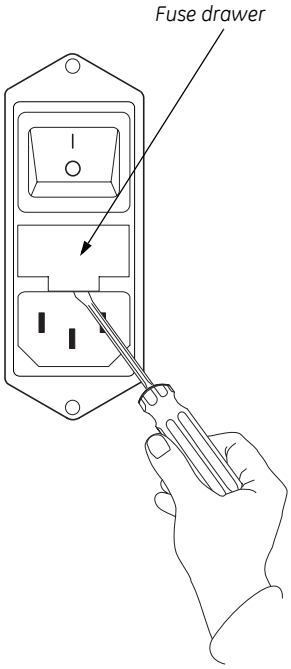
4 Insert a small screwdriver into the notch next to the fuse drawer.

5 Twist the screwdriver to open the fuse drawer.

6 Replace the fuse.

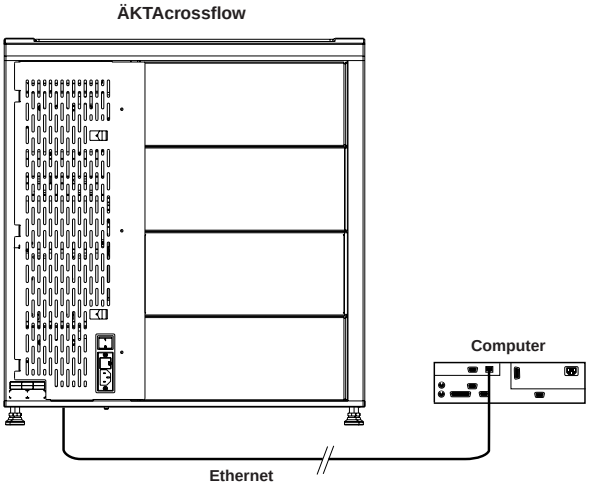
For fuse data, see section 5.3.1 Technical specifications.

7 Insert the fuse drawer into its receptacle on the connector panel.



5.1.6 UniNet-1 communication

The UniNet-1 data communication cable is connected internal to the CU-950, and from the CU-950 via Ethernet for external data communication, see figure below.



5.1.7 System flow path

The following flow diagram shows the positions of the components and tubing in the ÄKTAcrossflow liquid flow path.

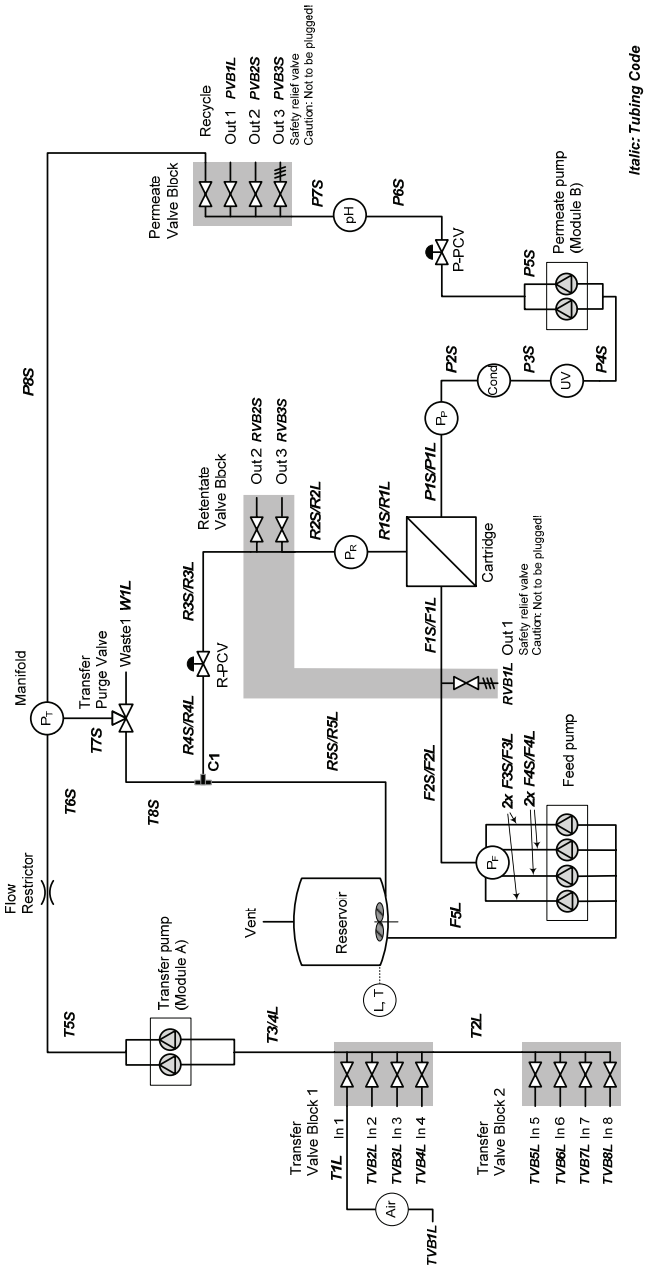


Fig 5-22. Liquid flow path.

Tubing	Length [mm]	I.d. [mm]	Material	Location	
				From	To
F5L	660 M	2.9	PVDF	Reservoir (outlet port)	Feed pump inlets
F3S	155	1.7	PVDF	Feed pump A (left, upper)	Sensor P_F inlet
				Feed pump B (right, upper)	Sensor P_F inlet
F3L	150	2.9	ETFE	Feed pump A (left, upper)	Sensor P_F inlet
				Feed pump B (right, upper)	Sensor P_F inlet
F4S	110	1.7	PVDF	Feed pump A (right, upper)	Sensor P_F inlet
				Feed pump B (left, upper)	Sensor P_F inlet
F4L	110	2.9	ETFE	Feed pump A (right, upper)	Sensor P_F inlet
				Feed pump B (left, upper)	Sensor P_F inlet
F2S	110	1.7	PVDF	Valve block R-VB	Sensor P_F outlet
F2L	95	2.9	ETFE		
F1S/ F1L	See Table 2-2 and Table 2-5				
R1S/ R1L	See Table 2-2 and Table 2-5				
R2S	110	1.7	PVDF	Sensor P_R, outlet	Valve block R-VB (left port)
R2L	95	2.9	ETFE		
R3S	200	1.7	PVDF	Valve block R-VB (right port)	Valve R-PCV (inlet port)
R3L		2.9	ETFE		
R4S	120	1.7	PVDF	Valve R-PCV (outlet port)	Connector C1
R4L		2.9	ETFE		
R5S	200	1.7	PVDF	Connector C1	Reservoir, inlet port
R5L		2.9	ETFE		
P1S/P1L	See Table 2-2 and Table 2-5				
P2S	170 pf	1.7	PVDF	Sensor P_P outlet	Conductivity cell inlet
P3S	200 pf	1.7	PVDF	Conductivity cell, outlet	UV cell, inlet
P4S	200 M	1.7	PVDF	UV cell, outlet	Permeate pump inlets
P5S	477 M	1.7	PVDF	Permeate pump outlets	Valve P-PCV (inlet port)
P6S	120	1.7	PVDF	Valve P-PCV (outlet port)	pH cell, inlet
P7S	100 pf	1.7	PVDF	pH cell, outlet	Permeate valve block P-VB (left port)
P8S	380 pf	1.7	PVDF	Permeate valve block P-VB-Out (recycle port)	Sensor P_T
T1L	95	2.9	ETFE	Air sensor	Transfer valve block 1 T-VB-In (port 1)
T2L	200	2.9	ETFE	Valve block 2, outlet	Valve block 1, inlet
T3/T4L	610 M	2.9	ETFE	Valve block 1, outlet	Transfer pump A, inlets
T5S	200 M	1.7	PVDF	Transfer pump outlets	Flow restrictor, inlet
T6S	155 pf	1.7	PVDF	Flow restrictor, outlet	Sensor P_T
T7S	510 pf	1.7	PVDF	Sensor P_T	Transfer purge valve
T8S	120	1.7	PVDF	Transfer purge valve	Connector C1

Tubing	Length [mm]	I.d. [mm]	Material	Location	
				From	To
W1L	2000	2.9	ETFE	Transfer purge valve	Waste
TVB1L	600	2.9	ETFE		Air sensor
TVB2L*	1200	2.9	ETFE		Transfer valve block 1 T-VB-In (port 2)
TVB3L*	1200	2.9	ETFE		Transfer valve block 1 T-VB-In (port 3)
TVB4L*	1200	2.9	ETFE		Transfer valve block 1 T-VB-In (port 4)
TVB5L*	1200	2.9	ETFE		Transfer valve block 2 T-VB-In (port 5)
TVB6L*	1200	2.9	ETFE		Transfer valve block 2 T-VB-In (port 6)
TVB7L*	1200	2.9	ETFE		Transfer valve block 2 T-VB-In (port 7)
TVB8L*	1200	2.9	ETFE		Transfer valve block 2 T-VB-In (port 8)
RVB1L*	600	2.9	ETFE	Retentate valve block R-VB-Out (port 1 = pressure relief valve)	
RVB2S*	600	1.7	PVDF	Retentate valve block R-VB-Out (port 2)	
RVB3S*	600	1.7	PVDF	Retentate valve block R-VB-Out (port 3)	
PVB1L*	2000	2.9	ETFE	Permeate valve block P-VB-Out (port 1)	Waste
PVB2S*	600	1.7	PVDF	Permeate valve block P-VB-Out (port 2)	
PVB3S*	600	1.7	PVDF	Permeate valve block P-VB-Out (port 3 = pressure relief valve)	
AL600*	600	2.9	ETFE	Accessory outlet tubing	
AL2000*	2000	2.9	ETFE	Accessory outlet tubing	
AS600*	600	1.7	PVDF	Accessory outlet tubing	
* = Single nut					
M = Manifold (equivalent tubing length)					
pf = pre-formed tubing					

Table 5-12. Tubing description.

All tubings are pre-flanged. The tubing end is equipped with a UNF 5/16" male connector and an ethylenepropylene (EPDM) O-ring.

5.1.8 Piston rinsing system

The piston rinsing system tubing is connected to the rearmost holes on the pump heads. The following flow diagram and table show the tubing configuration of the piston rinsing system.

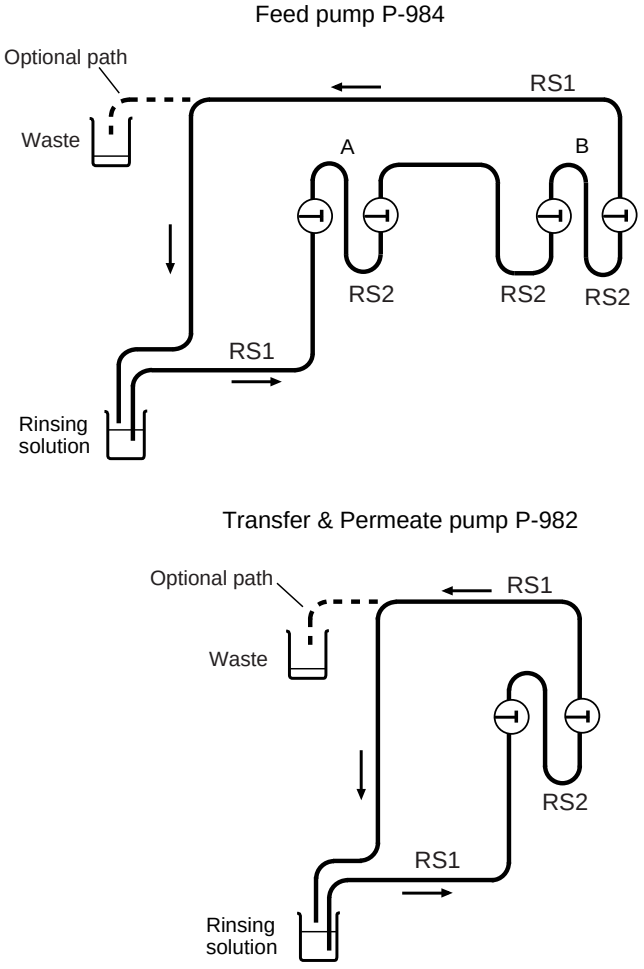


Fig 5-23. Piston rinsing system.

Tubing	Length [mm]	I.d. [mm]	Material	Location	
				From	To
RS1*	600	2.9	ETFE	Rinsing solution bottle	Transfer pump (left, lower)
RS2	300	2.9	ETFE	Transfer pump (left, upper)	Transfer pump (right, lower)
RS1*	600	2.9	ETFE	Transfer pump (right, upper)	Back to rinsing solution bottle (or waste)
RS1*	600	2.9	ETFE	Rinsing solution bottle	Permeate pump (left, lower)
RS2	300	2.9	ETFE	Permeate pump (left, upper)	Permeate pump (right, lower)
RS1*	600	2.9	ETFE	Permeate pump (right, upper)	Back to rinsing solution bottle (or waste)
RS1*	600	2.9	ETFE	Rinsing solution bottle	Feed pump A (left, lower)
RS2	300	2.9	ETFE	Feed pump A (left, upper)	Feed pump A (right, lower)
RS2	300	2.9	ETFE	Feed pump A (right, upper)	Feed pump B (left, lower)
RS2	300	2.9	ETFE	Feed pump B (left, upper)	Feed pump B (right, lower)
RS1*	600	2.9	ETFE	Feed pump B (right, upper)	Back to rinsing solution bottle (or waste)
* Single nut					

Table 5-13. Tubing description, piston rinsing system.

To use the piston rinsing system:

1 Fill the rinsing system bottles with 10 mM NaOH in 20% ethanol, see Fig 5-20.

2 Insert the rinsing inlet and outlet tubing ends into the rinsing solution, see Fig 5-23.

Note: *To eliminate the risk of re-introducing proteins/cells into the next batch run, always change rinsing solution.*

3 Fill the tubing with solution using a syringe connected to the outlet tubing end.

4 Repeat the procedure for all pumps.

Important! Always use the optional path (see Fig 5-23) if a continuous exchange of the rinsing solution is needed, i.e. re-circulation of the rinsing solution is not allowed.

5.2 Component descriptions

This section describes the components in the liquid flow paths of the ÄKTAcrossflow system.

5.2.1 Pump P-982 and P-984

Pump P-982 and P-984 are high performance laboratory pumps for use in applications where accurately controlled liquid flow is required. Twin reciprocating pump heads work in unison to deliver a smooth and pulse-free flow.

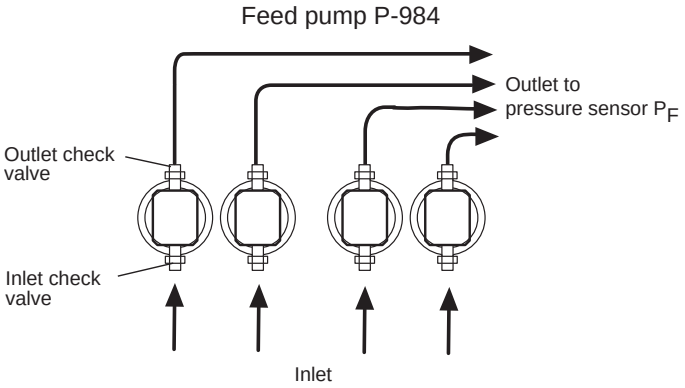
P-982 is used as the transfer pump (module A) and as the permeate pump (module B), P-984 is used as the feed pump (module A and B).

- Pump P-982 (two pump heads) features:
  - Pressure range 0–52 kPa (5.2 bar, 75.4 psi)
  - Flow rate range 0.1–200 ml/min
- Pump P-984 (four pump heads) features:
  - Pressure range 0–52 kPa (5.2 bar, 75.4 psi)
  - Flow rate range 1–600 ml/min

Pump heads

The individual pump heads are identical but are actuated in opposite phase to each other by individual stepper motors controlled by a microprocessor. This gives a continuous, low pulsation liquid delivery.

Each pump head is equipped with an inlet check valve and an outlet check valve for the liquid flow. In addition, each pump head has an outlet check valve for the rinsing system flow.



Solvent is drawn up into the pump head through a non-return inlet check valve by the action of the piston being withdrawn from the pump chamber.

On the delivery stroke of the piston, the inlet check valve is sealed by the pressure developed and buffer is forced out through a similar check valve at the outlet.

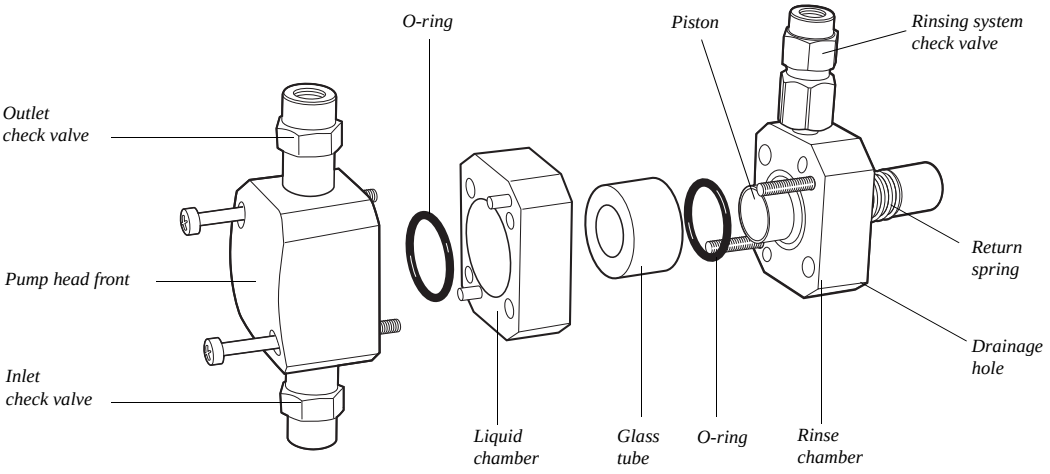


Fig 5-24. Pump head, exploded view

The pistons are actuated by cams (eccentrics) driven by the motors. Force for the retraction of the pistons is provided by coil springs. The length of stroke of the pistons is fixed and changes in the flow rate are made by varying the speed of the drive motor.

Leakage between the pump chamber and the drive mechanism is prevented by a piston. The piston is continuously lubricated by the presence of buffer. To prevent any deposition of salts from aqueous buffers on the pistons, the low pressure chamber behind the piston can be flushed continuously with a low flow of 10 mM NaOH in 20% ethanol.

The pump head is made of titanium alloy.

Pump principle

Each piston is driven by a simple robust cam (eccentric). These cams are driven by stepper motors via timing belts. The motor speed is varied to achieve linear movement and compensation for compressibility. This produces the particular motor sound. This system guarantees an accurate, low pulsation flow over the entire flow rate range, independent of the back pressure. When an increase in flow rate is programmed, the motor speed accelerates gradually, giving a soft start and building up speed to the flow rate required. When a decrease in flow rate is programmed, the motor speed slows rapidly to the lower flow rate.

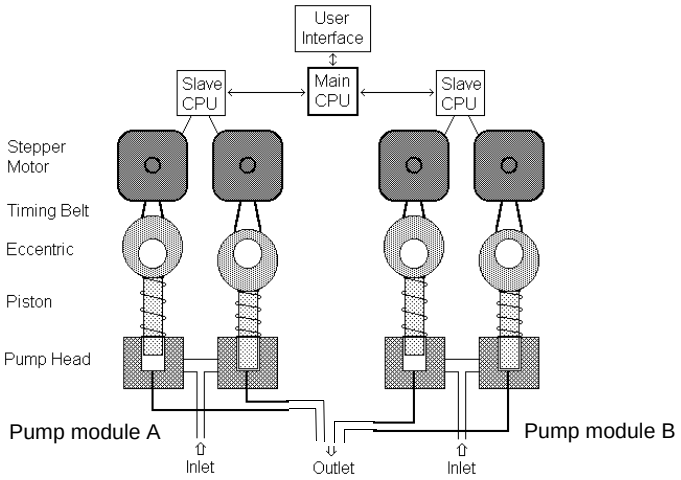
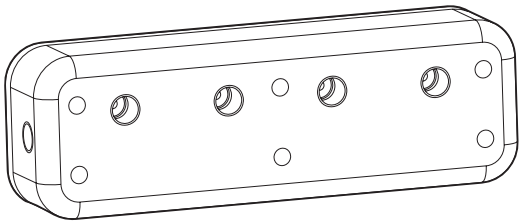


Fig 5-25. Feed pump P-984 pump principle.

5.2.2 Valves

Membrane valves

Each valve block comprises three or four stepper-motor actuated membrane valves with open/close functionality. The valves are located in valve blocks to minimize hold-up volumes and dead volumes.



A valve block consists of a connection block containing the ports and the membranes, and a mechanical housing containing the stepper motors, cams and actuating pistons. The membranes are made of EPDM.

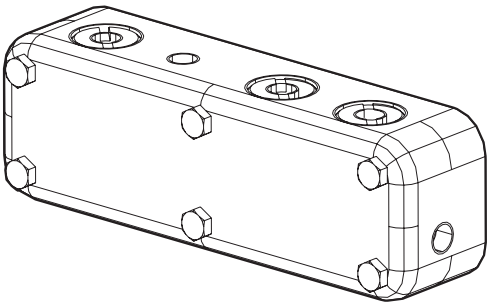
The valve blocks have different numbers of inlet and outlet ports depending on their position in the flow path.

- Inlet valves T-VB-In: 1–4
- Inlet valves T-VB-In: 5–8
- Outlet valves P-VB-Out: recycle, 1, 2, 3 (pressure relief valve)

One of the outlet valves, P-VB-Out 3, is used as pressure relief valve with the opening pressure 7 bar (102 psi).

Rocker valve

The valve block comprises three stepper-motor actuated diaphragm open/close valves. The diaphragm valve type comprises a membrane coated rocker.



The rocker closes against the flow through the inlet port with the closing force controlled by the stepper-motor. This design results in linear control characteristics of the valve.

The valve block has different numbers of inlet and outlet ports depending on their position in the flow path.

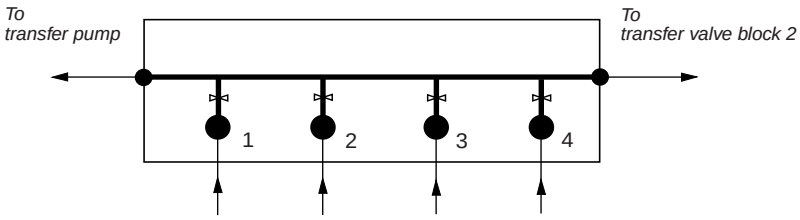
- Outlet valves R-VB-Out: 1 (pressure relief valve), 2, 3.

One of the outlet valves, R-VB-Out 1, is used as pressure relief valve with the opening pressure 7 bar (102 psi).

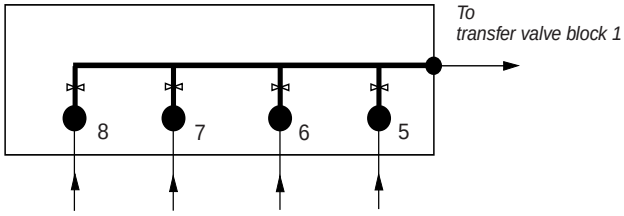
Valve block types

There are four different types of membrane valve blocks. The following illustrations show the flow path in the valve blocks and where the valves are located. The valves are normally closed.

- Transfer valve block 1, T-VB-In 1, 2, 3 and 4

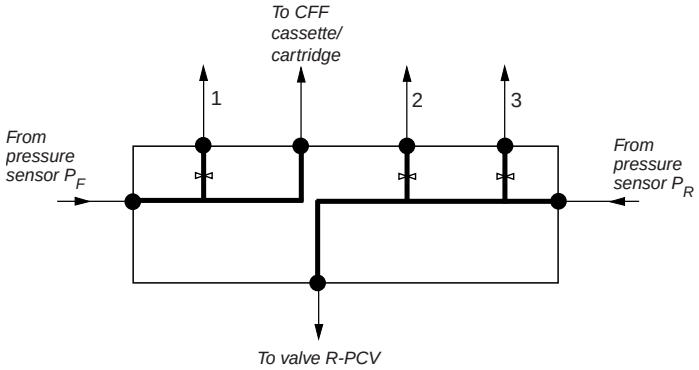


- Transfer valve block 2, T-VB-In 5, 6, 7 and 8

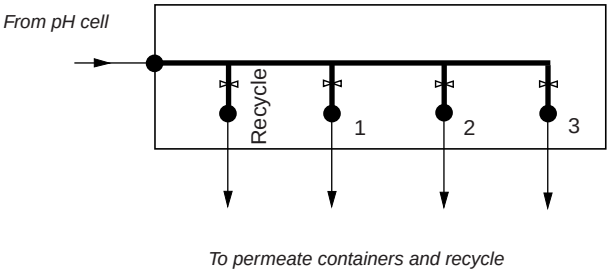


Note: *In transfer valve block 1 and 2, only one valve can be open at a time.*

- Retentate valve block, R-VB-Out 1, 2 and 3



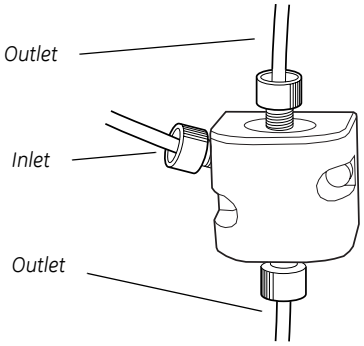
- Permeate valve block, P-VB-Out 1, 2, 3 and recycle



The valve blocks have UNF 5/16" female ports.

2-way transfer purge valve

The 2-way valve is of diaphragm type and comprises a membrane coated rocker. Actuated by a solenoid, the rocker blocks one of the two outlet ports in a flip-flop manner.

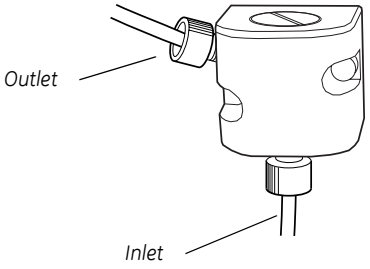


The inlet port is positioned at the side of the valve body, while the outlet ports are positioned at the top and bottom of the valve body.

The transfer purge valve is directing the liquid flow either from transfer line or permeate recycle towards the reservoir (default) or waste.

Pressure modulating valves R-PCV and P-PCV

The pressure control valves enable a throttling of the liquid flow in order to raise the pressure upstream the valve.



Mechanically, these valves are similar to the 2-way valve such that the throttling of the flow is achieved by the membrane coated rocker. However, compared to the 2-way switch valve, the pressure control valve has only one inlet and one outlet port.

The rocker is closing against the flow through the inlet port with the closing force controlled by the solenoid. This design results in linear control characteristics of the valve. Furthermore, the pressure upstream the valve is maintained irrespective of changes in flow rate.

- **Retentate control valve (R-PCV)**

  The retentate control valve R-PCV is used to accurately control the retentate pressure over the pressure range 0.1-5.2 bar. Hereby, the transmembrane pressure (TMP) can be adjusted.

  In addition, the R-PCV can operate as open/close valve in product recovery and system cleaning procedures.

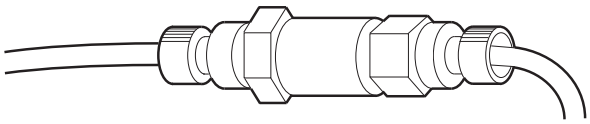
- **Permeate control valve (P-PCV)**

  The main task of the permeate control valve P-PCV is to modulate the pressure downstream the permeate pump in order to guarantee accuracy in the permeate flow rate.

  To ensure proper operation of the check valves, the pressure downstream the pump has to be greater than the pressure upstream the pump. Therefore, the P-PCV will be controlled such that it always maintains a higher pressure downstream the pump.

Flow restrictor in transfer line

A flow restrictor is positioned downstream the transfer pump in order to ensure a proper operation of the check valves at the pump heads. The restrictor generates a constant back pressure of min. 3 bar.



5.2.3 Reservoirs

The reservoir accommodates the liquid/sample to be processed. It provides a gentle, but efficient mixing of the process liquid with returning retentate and additional liquid added via the transfer line. Permeate may be recycled into the reservoir for achieving steady-state conditions during process development studies.

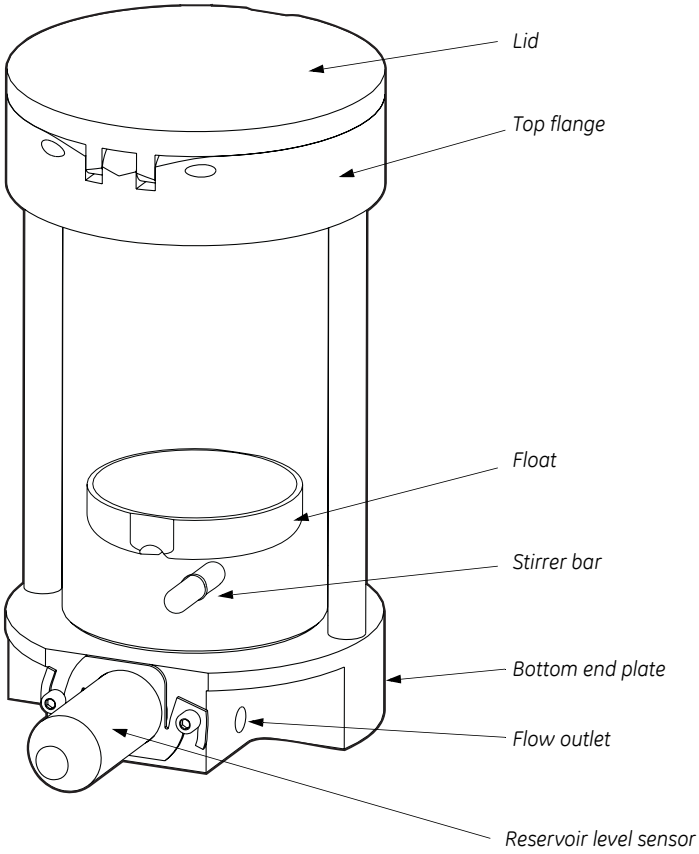


Fig 5-26. Reservoir 350 ml.

The reservoirs are equipped with a float to prevent vortex formation and foaming such that operation at lowest recirculation volume with high flow rate is facilitated.

There are two sizes of reservoirs:

- 350 ml (375 ml without float), mainly intended for UF/DF processes
- 1100 ml (1200 ml without float) (optional), mainly intended for MF processes

Each reservoir has connections for the liquid flow positioned at the reservoir bottom end plate. There is one outlet for delivering liquid to the feed pump via a manifold. The outlet is placed off-centre at the bottom of the reservoir to prevent vortex formation. The outlet is connected to a conduit/manifold that distributes the liquid to the four pump heads of the feed pump. The retentate return is positioned such that liquid is injected tangentially to the bottom surface.

The lid can be easily opened, for example for manual sampling of the retentate. It also has a connection for ventilation.

To open the lid:

- Move the lower part of the jointed hook outwards while pushing slightly the lid downwards, see figure below.

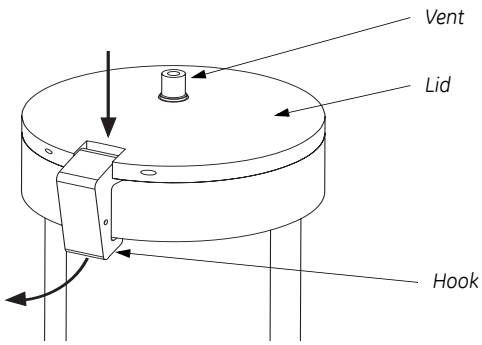


Fig 5-27. Reservoir lid.

The reservoir is mounted on a reservoir holder which comprises a motor unit for a magnetic stirrer-bar. The stirrer can be used with both reservoirs to improve mixing characteristics. Recommended dimensions for the stirrer are:

- 350 ml reservoir: length of stirrer 30 mm and o.d. 6 mm
- 1100 ml reservoir: length of stirrer 35 mm and o.d. 6 mm

The appropriate mixing rate is a function of application and retentate volume and can be adjusted by the control software. At low retentate volume, the stirrer and the float will be in contact such that the stirrer will rotate the float.

Under these conditions, a low mixing rate is being selected as default by the control software. At higher retentate volume where the float is not in contact with the stirrer, the user can select a higher mixing rate. The following rates are recommended as maximum mixing rates that will ensure sufficient mixing for all conditions:

- 350 ml reservoir: 200 rpm
- 1100 ml reservoir: 300 rpm

As default, the UNICORN control software adjusts the mixing rate automatically depending on the actual retentate volume.

An air filter (vent filter) can be connected to the top of the reservoir, see Fig 5-26.

The reservoir consists of the following material:

- glass tube: borosilicate
- bottom end plate, top flange and lid: polyetherimide
- sealing lid: thermoplastic elastomer
- float: polypropylene
- stirrer: polytetrafluoroethylene

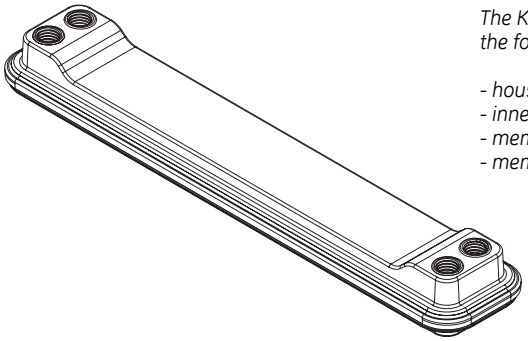
5.2.4 CFF cassette/cartridge

The CFF cassette/cartridge is the unit that encapsulates the filtration membrane.

Flat sheet membrane cassette

There are two main sizes of flat sheet membranes intended for UF/DF processes:

- 50 cm^2 membrane area, for typical feed flow rates of 25 to 40 ml/min – **Kvick Start**



The Kvick Start cassette consists of the following material:

- housing: epoxy
- inner flow plates: polypropylene
- membrane: polyethersulfone
- membrane screen: polypropylene

Fig 5-28. The Kvick Start cassette.

- 100 cm^2 membrane area, for typical feed flow rates of 60 to 80 ml/min – **Kvick Lab Packet**

The Kvick Lab Packet consists of the following material:

- holder: stainless steel
- membrane: polyethersulfone
- screen: polypropylene
- encapsulant: silicone
- gasket: silicone

Fig 5-29. The Kvick Lab Packet cassette.

Hollow fiber membrane cartridge

The hollow fiber cartridge consists of the following material:

- housing: polysulfone/polycarbonate
- membrane: polysulfone

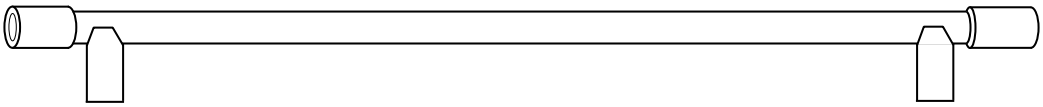


Fig 5-30. The hollow fiber membrane cartridge.

There are two main sizes of hollow fiber cartridges intended for UF/DF processes:

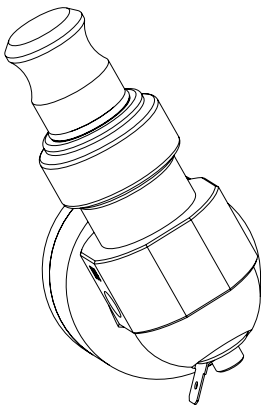
- 50 cm^2 membrane area with a fiber length of 30 cm for feed flow rates of 24 to 200 ml/min
- 40 cm^2 membrane area with a fiber length of 60 cm for feed flow rates of 10 to 85 ml/min

The hollow fiber cartridge size intended for MF processes:

- 50 cm^2 membrane area with a fiber length of 30 cm for feed flow rates of 70 to 560 ml/min

5.2.5 pH electrode and cell holder

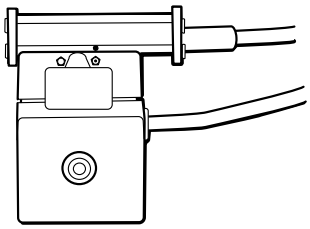
The pH electrode is optimized for continuous pH measurement in the ÄKTAcrossflow path. The electrode is of the sealed combination double junction type. It contains a sealed Ag/AgCl reference, which cannot be refilled, an internal electrolyte bridge of 4 M KCl saturated with Ag/AgCl, an outer electrolyte bridge of 1 M KNO_3, an annular ceramic reference junction and a low profile pH membrane.



The pH electrode has a glass tip and the cell holder is made of titanium. The whole assembly is replaceable.

The pH electrode should be calibrated regularly. This procedure is described in section 2.3.2.

5.2.6 Monitor UPC-980 and UV cell

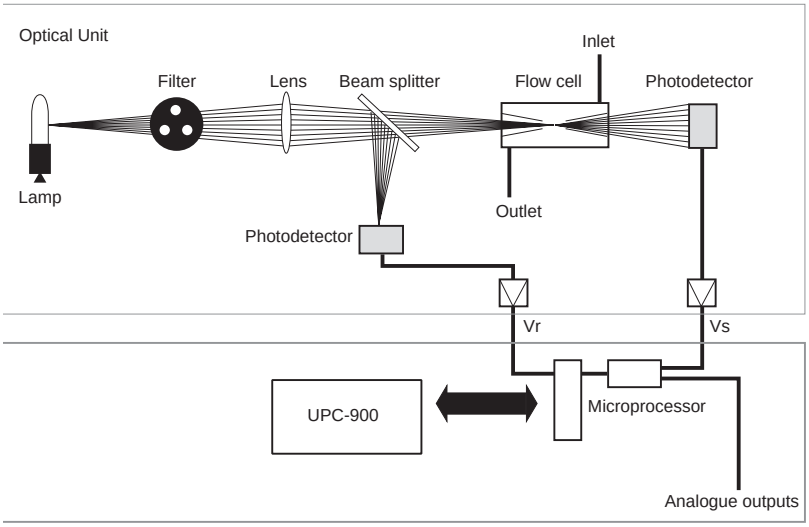


The UV cell is designed for continuous measurement of UV absorbance. The UV monitoring system provides high performance detection for the wavelengths 214, 254 and 280 nm.

The UV cell housing is made of PEEK, other wetted parts are made of glass and titanium.

UV optical unit

The UV optical unit houses the lamp (Zn or Hg), the wavelength filter and the UV flow cell. The light beam is directed through a flow-through cuvette to a photodetector. The photodetector current is fed to the signal processing circuitry in the module.



The reference signal comes from the same point in the lamp as the signal measuring the sample, thus assuring a stable baseline by eliminating the effects of variations in lamp intensity.

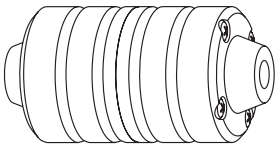
The Hg lamp emits light only at certain wavelengths. It does not emit light at 280 nm, so for this wavelength, the light is converted at a fluorescent surface before it passes the filter. On the lamp housing, there is a special exit for 280 nm light, which means that the lamp position needs to be changed when working with this wavelength.

For 214 nm wavelength, a Zn lamp is used. This lamp is larger than the Hg lamp and is therefore mounted in a larger lamp housing.

The lamp connectors are keyed to inform the monitor software of which lamp type is connected.

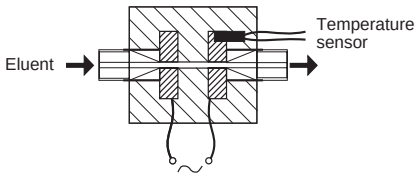
5.2.7 Conductivity cell

The cell has two cylindrical titanium electrodes positioned in the flow path of the cell. An alternating voltage is applied between the electrodes and the resulting current is measured and used to calculate the conductivity of the buffer. The system controls the AC frequency and increases it with increasing conductivity between 50 Hz and 50 kHz, giving maximum linearity and true conductivity values.



The conductivity is automatically calculated by multiplying the measured conductance by the cell constant of the cell. The cell constant is pre-calibrated on delivery but can be measured with a separate calibration procedure. This procedure is described in section 2.3.3.

One of the electrodes has a small temperature sensor for measuring the temperature of the buffer in the cell. Temperature variations influence the conductivity and in some applications, when very precise conductivity values are required, it is possible to program a temperature compensation factor that recalculates the conductivity to a set reference temperature.

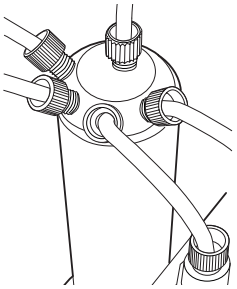


5.2.8 Pressure sensors

ÄKTAcrossflow system is equipped with four pressure sensors and one level sensor:

Pressure sensor P_F

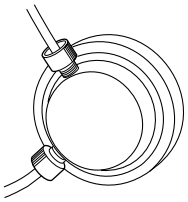
- Sensor P_F, located close to the CFF cassette/cartridge in the feed line to measure the feed pressure.



Pressure sensor P_F

Pressure sensors P_R and P_P

- Sensor P_R, located close to the CFF cassette/cartridge in retentate line to measure the retentate pressure.
- Sensor P_P, located close to the CFF cassette/cartridge in the permeate line to measure the permeate pressure.

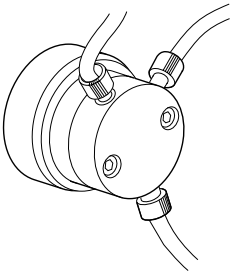


Pressure sensors P_R and P_P

Pressure sensor P_T

- Sensor P_T, located upstream the reservoir, is mainly used to measure the pressure in the reservoir for safety reasons.

  The liquid chamber in the P_T sensor housing is equipped with a thin titanium membrane. A strain gauge is attached to the rear side of the membrane. When the liquid pressure increases, the titanium membrane bulges, which is detected by the strain gauge.



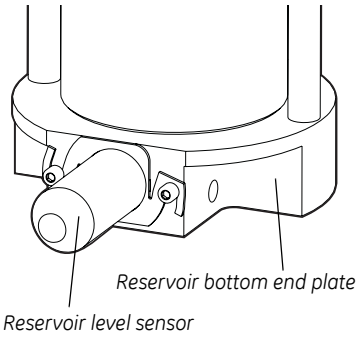
Pressure sensor P_T

The pressure is shown on the computer display. To protect the system, a maximum and minimum pressure limit can be set in UNICORN for pressure sensors P_F, P_R and P_P.

The pressure sensors have a pressure range of 0–10 bar (100 kPa, 145 psi). The pressure sensor housing is made of PEEK, other wetted parts are made of titanium and stainless steel.

Reservoir level sensor

- Level sensor, located in the reservoir bottom end plate. The level sensor also has the function of low volume alarm for the reservoir.



  The signal of the level sensor is used to calibrate the volume of the ÄKTAcrossflow system during start-up. Furthermore, the level sensor facilitates efficient product removal procedures at the end of the filtration process in case that any entrainment of air in the recirculation line is not desirable.

  The level sensor has a pressure range of 0–100 mbar (10 kPa, 1.45 psi).

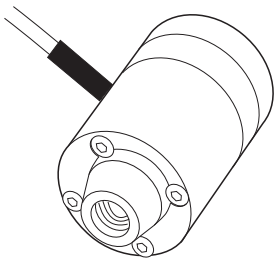
  A temperature sensor is integrated with the reservoir level sensor, and allows for continuous measurement of the liquid feed to the CFF cassette/cartridge.

CAUTION! The reservoir level sensor is highly sensitive. Do not insert any objects into the cavity in the bottom end plate of the reservoir since this may damage the level sensor.

5.2.9 Air sensor 925

Sample inlet air sensor

The sample air sensor is a high precision monitor designed for continuous monitoring of air bubbles in the flow path for the sample inlet. The air sensor is made of PEEK.



The air sensor ensures that the maximum volume of external feed can be transferred into the system without any risk for introducing air into the transfer line. When air is detected, the system is either paused, or performs an action that is set in the method.

Avoiding air in the transfer line is important to ensure the high volume accuracy of the transfer pump and thereby the accuracy of the retentate volume content.

5.3 Specifications

5.3.1 Technical specifications

ÄKTAcrossflow instrument unit

Mains voltage	100–240 V~ ±10%, 50–60Hz (Auto range) (Installation category II)
Power consumption	900 VA
Fuse specification, internal	T8.0 AH 250 Vac
Degree of protection	IP 20
Dimensions, instrument unit	650 × 620 × 400 mm (H × W × D)
Weight, instrument unit	70 kg
System holdup volume	18.2 – 25.8 ml depending on tubing kit
Operating temperature	4–40 °C (Max 50 °C for wetted parts during cleaning procedures)
Relative humidity, operation	20–95% (non-condensing)
Cabinet material	Aluminum
Safety standards	This product meets the requirements of the Low Voltage Directive (LVD) 73/23/EEC through the following harmonized standard: • EN 61010-1
EMC standards	This product meets the requirements of the EMC Directive 89/336/EEC through the following harmonized standard: • EN 61326 (emission and immunity)

Transfer pump and permeate pump P-982

Flow rate	0.1–200 ml/min
Increment	0.1 ml
Pressure	0–520 kPa (5.2 bar, 75.4 psi)
Flow rate accuracy	0.5% actual value within range (2–200 ml/min, 3.0–5.0 bar)
Pulsation *Permeate pump* *Transfer pump*	 Max. ±10% at inlet side (With inlet flow 10 ml/min, 4 bar) Max. ±20% at outlet side (With outlet flow 10 ml/min, 4 bar)
Flow rate reproducibility	rsd < 0.15% (0.1–200 ml/min, 3.0–5.0 bar)
Viscosity	0.8–5.0 cP
Internal volume	3050 µl incl. check valves

Feed pump P-984

Flow rate	1–600 ml/min
Increment	0.1 ml
Pressure	0–520 kPa (5.2 bar, 75.4 psi)
Pulsation	Max. ±10% at outlet side (With outlet flow 10 ml/min, 4 bar)
Flow rate accuracy	< ±2% (2–600 ml/min, 2.0–5.2 bar)
Flow rate reproducibility	rsd < 0.3% (2–600 ml/min, 2.0–5.2 bar)
Viscosity *1–600 ml/min*	 0.8–5.0 cP
Internal volume	6100 µl incl. check valves
Liquid exchange between product side and rinsing system	< 4.5 ppm of pumped volume

UV measurement, Monitor UV-980

UV cell path length	2 mm
UV cell flow area	1.6 mm^2
UV cell total holdup volume	0.21 ml
Baseline adjust	Adjustable 0–100% of full scale
UV cell max. pressure	1 MPa (10 bar, 145 psi)
Wavelength *Hg lamp* *Zn lamp*	 254 and 280 nm (other wavelengths optional) 214 nm
Static noise (Typical values at room temperature after warm-up. Time constant 1 s) *long-term* *short-term*	 40×10^{-6} AU at 254 nm 40×10^{-6} AU at 254 nm (typically 6×10^{-6} AU at 254 nm)
Static drift	$\pm 100 \times 10^{-6}$ AU/h at 254 nm
Autozero range	-0.2–2.0 AU
Absorbance range	0.01–5 AU

pH measurement, Monitor pH/C-980

pH range	0–14 (spec. valid between 2 and 12)
Accuracy *temperature compensated* *not temperature compensated*	 ±0.1 pH units within 4–40 °C ±0.2 pH units within 15–25 °C ±0.5 pH units within 4–15 °C and 25–40 °C
Response time	Max. 10 s (0–95% of step)
Long-term drift	Max. 0.1 pH units/10 h
Flow rate sensitivity	Max. 0.1 pH units within 0-100 ml/min.
Max. pressure	0.5 MPa (5 bar, 72 psi)
Internal volume, pH cell holder	240 µl

Conductivity measurement, Monitor pH/C-980

Conductivity range	1 µS/cm to 250 mS/cm
Deviation from theoretical conductivity	Max. ±2% of full scale calibrated range or ±10 µS/cm whichever is greater in the range 1 µS/cm to 250 mS/cm
Reproducibility *short-term* *long-term*	 Max. ±1% or ±5 µS/cm Max. ±3% or ±15 µS/cm
Noise	Max. ±0.5% of full scale calibrated range
Response time	Max. 3 s (0–95% of step)
Flow rate sensitivity	±1% within 0–400 ml/min
Max. pressure	2 MPa (20 bar, 290 psi)
Internal volume, conductivity cell	180 µl

Membrane valves

Max. pressure	520 kPa (5.2 bar, 75.4 psi)
Internal volume *T-VB 1 and 2* *P-VB*	 570 µl (closed) 570 µl (closed)
Valve principle	Stepper motor-controlled membrane

Rocker valve

Max. pressure	520 kPa (5.2 bar, 75.4 psi)
Internal volume *R-VB, retentate side* *R-VB, feed side*	 540 µl (closed) 390 µl (closed)
Valve principle	Stepper motor-controlled rocker

Control valves R-PCV and P-PCV

Max. pressure	520 kPa (5.2 bar, 75.4 psi)
Internal volumes: *P-PCV* *R-PCV*	 540 µl, 520 µl (closed) 540 µl, 520 µl (closed)
Valve principle	Solenoid-actuated rocker

Flow restrictor (Transfer line)

Back pressure	Min. 3 bar
Internal volume	570 µl
Valve principle	Spring-loaded cone

Transfer purge valve

Max. pressure	520 kPa (5.2 bar, 75.4 psi)
Internal volume	600 µl, 580 µl (closed)
Valve principle	Solenoid-actuated rocker, membrane coated

Reservoirs

Max. volume *Without float* *With float*	 375 ml, 1200 ml 350 ml, 1100 ml
Mixing principle	Magnetic stirrer

Pressure sensors P_F, P_R, P_P

Pressure range	Up to 1 MPa (10 bar, 145 psi)
Pressure accuracy	±0.01 bar
Internal volume: P_F P_R, P_P	 565 µl 340 µl

Pressure sensor P_T

Pressure range	0–2.5 MPa (25 bar, 362 psi)
Pressure accuracy	< ±2%
Internal volume	294 µl

Reservoir level sensor

Pressure range	0–100 mbar (10 kPa, 1.45 psi)
Reproducibility in empty reservoir detection	±0.2 ml
Drift under constant retentate volume operation	±0.1 mbar (10 Pa) over 4 hours, valid for temperature changes ≤ 1 °C/hour (for water, a hydrostatic pressure of 10 Pa corresponds to approx. 2.8 ml in the small reservoir, and 6.4 ml in the large reservoir)

*Temperature sensor**

Accuracy	±1 °C (valid for temperature difference < 5 °C between liquid temperature and ambient temperature)
*Integrated with reservoir level sensor	

Air sensor 925

Max. pressure	2.5 MPa (25 bar, 362 psi)
Internal volume	190 µl

Table 5-14. ÄKTAcrossflow technical specification

5.3.2 ÄKTAcrossflow component materials

The wetted materials of ÄKTAcrossflow are listed below:

	PEEK	PTFE	FFKM	ETFE	CTFE	PP	PVDF	UHMWPE	EPDM	PEI	Borosilicate (glass)	Elgiloy	Ruby	Polyethersulfone	Polycarbonate	Titanium alloy	Zirconia	Suprasil 2	TPE	Stainless steel
Pumps (feed, transfer and permeate)	X		X					X			X	X	X			X	X			
UV cell	X			X												X		X		
pH cell holder/dummy electrode		X	X													X				
Conductivity cell					X											X				
Flow restrictor (transfer line)	X																			X
Valve blocks (transfer, permeate)	(X)								X	X										
Valve block (retentate)									X	X										
Pressure control valves									X	X										
Pressure sensors (feed, retentate and permeate)	(X)								X	X										X
Pressure sensor, transfer	X															X				
Air sensor	X																			
Tubing				X			X		X											
Unions/connectors	X																			
Reservoirs									X	X	X								X	
Reservoir float						X														
Reservoir level sensor																				X
CFF cassettes/cartridges						X								X	X					
Stirrer		X																		
Transfer purge valve									X	X										
Bottles											X									

FFKM = perfluoro elastomer
PEEK = polyetheretherketone
PVDF = polyvinylidene fluoride
PEI = polyetherimide
PP = polypropylene
Elgiloy = cobalt-chromium-nickel alloy
(X) = alternative material
CTFE = polychlorotrifluoroethylene
PTFE = polytetrafluoroethylene
ETFE = ethylene tetrafluoroethylene
EPDM = ethylene propylene diene monomer
TPE = thermoplastic elastomer
UHMWPE = ultrahigh molecular weight polyethylene
Suprasil 2 = Fused silica

Table 5-15. Wetted materials in ÄKTAcrossflow.

5.4 Chemical resistance guide and chemical compatibility

The resistance of construction materials varies with chemical concentration, exposure time, and exposure temperature. The following list provides an indication of the resistance of the ÄKTAcrossflow components to common chemicals and cleaning agents at room temperature.

However, before a filtration run, the chemical resistance of the CFF cassettes/cartridges must be checked with the chemical compatibility list provided with the cassette/cartridge.

The ratings are based on the following assumptions:

1 The synergistic effects of chemical mixtures have not been taken into account.

2 Room temperature (unless otherwise stated) and limited over-pressure are assumed.

Note: *Chemical influences are time and pressure dependent. Unless otherwise stated, all concentrations are 100%.*

CAUTION! The chemicals listed in the table below are not valid for CFF cassettes/cartridges.

Chemical	*Exposure < 1 day*	*Exposure up to 2 months*	*Comments*
Acetic acid, < 5%	OK	OK*	Stainless steel is affected
Acetic acid, 70%	OK*	Avoid	EPDM and stainless steel are affected
Acetone, 10%	OK	Avoid	PEI is affected
Acetonitrile, 10%	OK	Avoid	EPDM, TPE, PP and PE are affected
Ammonia, 5%	OK	OK	
Ammonium chloride	OK*	Avoid	Stainless steel is affected
Ammonium sulphate	OK*	Avoid	Stainless steel is affected
Citric acid	OK	OK	
Detergents	OK	OK	
Ethanol, < 50%	OK	Avoid	TPE and EPDM are affected
Ethanol, > 50%	Avoid	Avoid	TPE and EPDM are affected
Ethanol, 20%	OK	OK	For storage
Ethylene glycol	OK	OK	
Glycerol	OK	OK	
Guanidinium hydrochloride	OK*	OK*	
Hydrochloric acid, 0.1 M	OK*	Avoid	Stainless steel is affected

Chemical	*Exposure < 1 day*	*Exposure up to 2 months*	*Comments*
Hydrochloric acid, > 0.1 M	Avoid	Avoid	Stainless steel and titanium are affected
Isopropanol, < 50%	OK	Avoid	TPE and EPDM are affected
Isopropanol, > 50%	Avoid**	Avoid	TPE and EPDM are affected
Methanol, < 50%	OK	Avoid	TPE and EPDM are affected
Methanol, > 50%	Avoid	Avoid	TPE and EPDM are affected
Nitric acid, 0.5 M	OK	Avoid	EPDM and stainless steel are affected
Phosphoric acid, 10%	OK*	Avoid	Titanium, aluminium oxide, glass and stainless steel are affected
Peracetic acid, 3%	OK	Avoid	
Potassium chloride	OK*	OK*	Stainless steel is affected
Sodium acetate	OK*	OK*	
Sodium bisulphate	OK*	OK*	Stainless steel is affected
Sodium chloride	OK*	OK*	Stainless steel is affected
Sodium hydroxide, 2 M	OK	Avoid	PVDF and borosilicate glass are affected
Sodium hydroxide, 1 M, 50 °C	OK	Avoid	PVDF and borosilicate glass are affected
Sodium hydroxide + sodium hypochloride (1.0 M + 500 ppm) 50 °C	OK	Avoid	PVDF and borosilicate glass are affected
Sodium hypochloride, 500 ppm, 50 °C	OK	Avoid	Stainless steel is affected
Sodium sulphate	OK	OK	
Sulphuric acid, 0.5 M	OK*	Avoid	EPDM, PEEK, PEI and titanium are affected
Urea	OK*	OK*	

* Limited suitability at low pH (pH < 4 is not recommended for stainless steel)

** OK for membrane rinsing/wetting procedures, short time

5.5 Ordering information

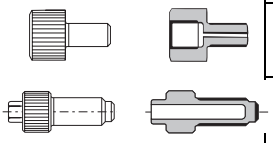
A selection of inlet and outlet tubing and connectors are included in the delivery of ÄKTAcrossflow. The items listed in below can be ordered from your local GE Healthcare representative.

Item	Quantity/ pack	Code no.
Feed pump/Transfer pump/Permeate pump		
Pump head 400 ml cpl, including piston assembly, O-rings (2 pcs), glass tube, liquid chamber, pump head front, 3 check valves	1	18-1169-87
Piston assembly 400 ml cpl, including rinsing chamber, piston, sealing, O-ring, check valve adapter	1	18-1169-90
Glass tube	1	18-1169-92
Check valve, inner, cpl	1	18-1169-88
Check valve, outer, cpl	1	18-1169-89
Seal kit, 400 ml	1	18-1169-91
pH monitoring		
pH electrode, including O-ring and nut	1	18-1168-77
Cell holder, pH	1	18-1170-02
Dummy pH electrode, incl. O-ring and nut	1	18-1169-11
O-ring	1	18-1118-60
pH calibration kit	1	11-0027-16
pH calibration bracket	1	11-0027-13
Conductivity monitoring		
Conductivity cell, i.d. 2.5 mm	1	18-1169-00
Cell holder, air sensor/cond	1	18-1170-01
UV monitoring		
UV flow cell, 2 mm 5/16 cpl	1	11-0031-48
O-ring kit	1	18-3685-01
Hg optics with 254, 280 nm filters	1	18-1128-20
Zn optics with 214 nm filter	1	18-1128-21
Hg lamp & housing cpl	1	18-1128-22
Zn lamp & housing cpl	1	18-1128-23
Filter 214 nm	1	18-0622-01
Filter 254 nm	1	18-0620-01
Filter 280 nm	1	18-0621-01
Filter 313 nm	1	18-0623-01

Item	Quantity/ pack	Code no.
Filter 365 nm	1	18-0624-01
Filter 405 nm	1	18-0625-01
Filter 436 nm	1	18-0626-01
Filter 546 nm	1	18-0627-01
Reservoir		
Reservoir cpl, 375 ml	1	11-0031-46
Reservoir cpl, 1200 ml	1	11-0031-16
Stirrer, 30 × 6 mm	2	11-0027-21
Stirrer, 35 × 7 mm	2	11-0027-22
Air filter	1	11-0027-18
Reservoir cleaning kit	1	11-0033-86
Air sensor		
Cell 925	1	18-1167-70
Membrane valve		
Connection block T-VB1	1	28405594
Connection block T-VB2	1	28405595
Connection block P-VB	1	28405597
Valve membrane	4	11-0031-43
Rocker valve		
Connection block R-VB	1	28405596
Rocker	3	11-0033-62
Control valves R-PCV and P-PCV		
Valve, cpl	1	11-0026-70
Rocker	1	11-0033-62
2-way transfer purge valve		
Valve, cpl	1	11-0026-71
Rocker	1	11-0033-62
Flow restrictor		
Valve, cpl	1	11-0026-72
Pressure sensors		
Pressure sensor P_T, 2.5 MPa, including outlet manifold	1	18-1169-79
Pressure sensor P_F, P_P, P_R	1	11-0026-66

Item	Quantity/ pack	Code no.
Flat sheet membrane cassettes		
Kvick Start™, 50 cm^2, 5 kD, PES UFEST0005050ST	1	11-0006-02
Kvick Start, 50 cm^2, 10 kDs, PES UFEST0010050SE	1	11-0006-04
Kvick Start, 50 cm^2, 10 kD, PES UFEST0010050ST	1	11-0006-03
Kvick Start, 50 cm^2, 30 kD, PES UFEST0030050ST	1	11-0006-05
Kvick Start, 50 cm^2, 50 kD, PES UFEST0050050ST	1	11-0006-06
Kvick Start, 50 cm^2, 100 kD, PES UFEST0100050ST	1	11-0006-08
Kvick Start CPACK, 50 cm^2 5 kD, 10 kD, 10 kDs, 30 kD, 50 kD, 100 kD UFESTCPAK045ST	1 of each membrane type	11-0006-61
Kvick Lab Packet, 100 cm^2, 10 K S UFELA0010001SE	1	11-0006-70
Hollow fiber membrane cartridges		
HF Start AXH, 40 cm^2, 3 kD, 0.5 mm UFP-3-C-H24U	1	11-0005-37
HF Start AXH, 40 cm^2, 10 kD, 0.5 mm UFP-10-C-H24U	1	11-0005-38
HF Start AXH, 40 cm^2, 30 kD, 0.5 mm UFP-30-C-H24U	1	11-0005-39
HF Start AXH, 40 cm^2, 100 kD, 0.5 mm UFP-100-C-H24U	1	11-0005-40
HF Start AXH, 40 cm^2, 300 kD, 0.5 mm UFP-300-C-H24U	1	11-0005-41
HF Start AXH, 40 cm^2, 500 kD, 0.5 mm UFP-500-C-H24U	1	11-0005-42
HF Start AXM, 50 cm^2, 3 kD, 0.5 mm UFP-3-C-2U	1	11-0005-43
HF Start AXM, 50 cm^2, 10 kD, 0.5 mm UFP-10-C-2U	1	11-0005-44
HF Start AXM, 50 cm^2, 30 kD, 0.5 mm UFP-30-C-2U	1	11-0005-45
HF Start AXM, 50 cm^2, 100 kD, 0.5 mm UFP-100-C-2U	1	11-0005-46

Item	Quantity/ pack	Code no.
HF Start AXM, 50 cm^2, 300 kD, 0.5 mm UFP-300-C-2U	1	11-0005-47
HF Start AXM, 50 cm^2, 500 kD, 0.5 mm UFP-500-C-2U	1	11-0005-48
HF Start AXM, 50 cm^2, 500 kD, 1 mm UFP-500-E-2U	1	11-0005-49
HF Start AXM, 50 cm^2, 750 kD, 1 mm UFP-750-E-2U	1	11-0005-50
HF Start AXM, 50 cm^2, 0.1 µm, 1 mm CFP-1-E-2U	1	11-0005-51
HF Start AXM, 50 cm^2, 0.2 µm, 1 mm CFP-2-E-2U	1	11-0005-52
HF Start AXM, 50 cm^2, 0.45 µm, 1 mm CFP-4-E-2U	1	11-0005-53
HF Start AXM, 50 cm^2, 0.65 µm, 0.75 mm CFP-6-D-2U	1	11-0005-54
HF Start AXM PACK, 50 cm^2 750 kD, 0.1 µm, 0.2 µm, 0.45 µm, 0.65 µm	1	11-0005-65
Connectors and unions		
T-connection 5/16" female	2	18-1170-59
Union 5/16" female-luer male	5	11-0027-07
Union Luer-lock female–M6 female	2	18-1027-12
Union 5/16" female/M6 male	3	18-1127-76
Stop plug, 5/16"	5	18-1112-50
Connector UNF 5/16" female	5	18-1173-51
Connector TC-5/16" female	2	18-1169-22
TC gasket 25/6.5 mm	4	18-1169-25
Tubing		
Recirculation line, large i.d. tubing kit	1	11-0031-30
Recirculation line, small i.d. tubing kit	1	11-0031-21
Recirculation manifold	1	11-0031-49
Rinsing tubing kit	1	11-0031-27
Inlet/outlet tubing kit	1	11-0031-28
Transfer/permeate tubing kit	1	11-0031-29
Accessory outlet tubing kit	1	11-0031-22



Item	Quantity/ pack	Code no.
Delivery tubing tubing kit	1	11-0031-23
O-ring 3 × 1 mm	50	11-0025-47
Bottles		
Screw lid GL45 kit	1	11-0004-10
Tubing lock GL45 cap	6	11-0012-52
Bottle holder	1	11-0027-12
Miscellaneous		
Tubing cutter	1	18-1112-46
Tool kit	1	11-0027-14
Air filter	1	11-0027-18
Sample holder, one tube (Falcon)	1	11-0027-15
Sample holder, two tubes	1	11-0031-25
Bag holder	1	11-0031-24
Membrane holder	1	11-0031-44
Kvick Lab Packet holder KLPH001SSU	1	11-0006-70
Block, hollow fiber holder	1+1	11-0027-17
Cassette manifold kit	1	11-0031-53

Table 5-16. Ordering information.

Index

A
absorbance range 130
air filter 121
    ordering information 141
air sensor
    description 14, 127
    ordering information 138
    replacing 77
    specification 133
ÄKTAcrossflow system 3

B
bag holder
    ordering information 141
baseline drift
    conductivity curve 90
block, hollow fiber holder
    ordering information 141
bottles 101
    ordering information 141
buffer bag holder 100

C
calibrating
    conductivity cell 43
    pressure sensor PT 40
    reservoir level sensor 45
    temperature sensor 42
cartridge 12, 122
    connecting 34
    preparing for use 33
cassette 12, 122
    connecting 28, 32
    preparing for use 27
cassette manifold
    connecting 31
cassette manifold kit
    ordering information 141
cell constant 42
    calibrating 43
check list, before run 37
check valves
    replacing 65
cleaning
    check valves 56
    conductivity cell 60
    membrane valves 58
    pH electrode 59
    pressure sensor 60
    sample inlet air sensor 61
    the system 55
    UV cell 58
compensation factor
    conductivity cell 42
components
    materials 134
    positions in the liquid flow path 106
conductivity cell 14
    calibrating 42
    calibration interval 39
    cleaning 60
    maintenance 54
    ordering information 137
    replacing 84
conductivity curve
    troubleshooting 90
conductivity temperature compensation 42
connectors 14
    ordering information 140
control valves
    ordering information 138
    specifications 131
cross flow filtration (CFF) 1

D
degree of protection 128
dimensions, filtration unit 128
documentation 19

E
EMC standards 128

F
feed pump
    maintenance 53
    ordering information 137
    replacing 62
flat sheet membrane 12, 122
    ordering information 139
flow path 106
flow rate
    accuracy 129
    feed pump 8
    permeate pump 8
    range, feed pump 129
    range, transfer pump and permeate pump 129
    reproducibility 129
    transfer pump 8
flow restrictor 10, 118
    ordering information 138
    specification 132
fraction collector 17

fuse specification 128

G
ghost peaks
UV curve 91

H
holdup volume 48, 128
hollow fiber membrane 12, 123
ordering information 139

I
indicator
power 98
the run indicator in UNICORN 23
installation category 128

K
Kvick Lab Packet 12, 122
connecting 32
Kvick Lab Packet holder
ordering information 141
Kvick Start 12, 122
ordering information 139

L
lifting instructions 51

M
mains cable 103
mains fuse 104
replacing 104
mains power switch 21, 98
mains voltage 128
maintenance
daily 52
measurement range
conductivity cell 14
pH electrode 13
UV flow cell 14
membrane holder
ordering information 141
membrane valve
description 9
membrane valves
cleaning 58
description 114
maintenance 54
ordering information 138
replacing 68
specifications 131
microfiltration 7
monitor pH/C-980
specifications 130
monitor UV-980
specifications 130
moving the system 51

N
noisy signal
pressure curve 90
UV curve 91

O
operating temperature 128
ordering information
air filter 141
air sensor 138
bag holder 141
block, hollow fiber holder 141
bottles 141
cassette manifold kit 141
conductivity cell 137
control valves 138
feed pump 137
flat sheet membrane 139
flow restrictor 138
hollow fiber membrane 139
Kvick Lab Packet holder 141
Kvick Start 139
membrane holder 141
membrane valves 138
permeate pump 137
pH electrode 137
pressure sensors 138
reservoir 138
rocker valve 138
sample holders 141
tool kit 141
transfer pump 137
tubing 140
UV cell 137

P
permeate control valve (P-PCV) 10
permeate line 6
permeate pump
maintenance 53
ordering information 137
replacing 62
pH cell holder
ordering information 137
replacing 83
pH electrode 13
calibrating with the electrode outside the flow cell 40
calibration interval 39
check before run 37
cleaning 59

maintenance 53
ordering information 137
regeneration 60
replacing 83
pH measurement 13
specifications 130
piston 112, 113
piston rinsing system
tubing configuration 109
power consumption 128
power indicator 21
preparing the system 37
pressure curve
checking 94
pressure relief valve 10, 114, 115
pressure sensor PT
specification 132
pressure sensors
calibration interval 39
cleaning 60
ordering information 138
replacing 74
sensor PT, calibrating 40
pressure sensors PF, PR, PP
specifications 132
preventive maintenance (PM) 86
priming the transfer pump 85
protein concentration 7
protein diafiltration 7
pump heads
description 111
pump P-982
specifications 129
pump P-984
principle 113
specifications 129

R

rating label 5
recirculation line 6
relative humidity 128
replacing
air sensor 77
check valves 65
conductivity cell 84
membrane valve block 68
pH electrode and cell holder 83
pressure sensors 74
rocker valve block 69
UV cell 78
reservoir 11, 119
maintenance 54
ordering information 138
selecting 24
reservoir level sensor
specification 133
reservoirs
specifications 132
retentate control valve (R-PCV) 10
rinsing system check valve 112
rocker valve 9, 114
description 114
ordering information 138
rocker valves
replacing 69

S

Safety standards 128
sample holders
ordering information 141
sample inlet air sensor 61
cleaning 61
sanitization of the flow path 18
starting ÄKTAcrossflow system 21
stepper motors 9, 114
stirrer 11, 120

T

temperature compensation 42
temperature sensor
calibrating 42
specification 133
tool kit
ordering information 141
trans membrane pressure (TMP) 1
transfer line 6
transfer pump
maintenance 53
ordering information 137
replacing 62
transfer purge valve 10
ordering information 138
specification 132
troubleshooting
air sensor 92
conductivity curve 90
feed pump, transfer pump and permeate pump 88
ghost peaks 91
membrane valves 89
pressure sensors 89
UV curve 91
tubing
check before run 37
configuration of the piston rinsing system 109
description 14, 108
ordering information 140
positions in the liquid flow path 106

tubing connections
maintenance 54
tubing kit
configurations 25
tubing kits 27
tubing lock 102

U
ultrafiltration 7
UNICORN 3
start and log on 22
UniNet-1 communication 105
unions
ordering information 140
user maintenance schedule 52
UV cell
cleaning 58
maintenance 53
replacing 78
specifications 130
UV curve
troubleshooting 91
UV flow cell 14
ordering information 137
UV measurement
specifications 130

V
valve block
description 114
viscosity 129

W
weight, instrument unit 128
wetted materials 134
working volume 48

For contact information for your local office, please visit www.gelifesciences.com/contact

GE Healthcare Bio-Sciences AB
Björkgatan 30
751 84 Uppsala
Sweden

www.gelifesciences.com

GE, imagination at work and GE monogram are trademarks of General Electric Company.

Drop Design, ÄKTAcrossflow, ÄKTA, UNICORN, Kvick Start and KVICK Lab Packet are trademarks of GE Healthcare companies.

UNICORN: Any use of this software is subject to GE Healthcare Standard Software End-User License Agreement for Life Sciences Software Products.

All third party trademarks are the property of their respective owners.

© 2004-2007 General Electric Company—All rights reserved.
First published Jan. 2004

All goods and services are sold subject to the terms and conditions of sale of the company within GE Healthcare which supplies them. A copy of these terms and conditions is available on request. Contact your local GE Healthcare representative for the most current information.

GE Healthcare UK Ltd
Amersham Place,
Little Chalfont,
Buckinghamshire, HP7 9NA,
UK

GE Healthcare Bio-Sciences Corp
800 Centennial Avenue,
P.O. Box 1327, Piscataway,
NJ 08855-1327,
USA

GE Healthcare Europe GmbH
Munzinger Strasse 5,
D-79111 Freiburg,
Germany

GE Healthcare Bio-Sciences KK
Sanken Bldg. 3-25-1,
Hyakunincho, Shinjuku-ku,
Tokyo 169-0073,
Japan

imagination at work

11-0012-33 AC 09/2007